N-SULFONYLATED PYRAZOLO[3,4-*b*]PYRIDIN-6-CARBOXAMIDES AND METHOD OF USE

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Application No. 62/239,647, filed October 9, 2015 and U.S. Provisional Application No. 62/309,794, filed March 17, 2016, both of which are incorporated herein by reference for all purposes.

BACKGROUND OF THE INVENTION

Technical Field

[0002] The invention relates to compounds that are modulators of the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) protein, useful in treating diseases and conditions mediated and modulated by CFTR. Additionally, the invention relates to compositions containing compounds of the invention and processes for their preparation.

Description of Related Technology

[0003] ATP-Binding Cassette ("ABC") transporters are a family of homologous membrane transporter proteins regulating the transport of a wide variety of pharmacological agents (for example drugs, xenobiotics, anions, etc.) that bind and use cellular adenosine triphosphate (ATP) for their specific activities. Some of these transporters were found to defend malignant cancer cells against chemotherapeutic agents, acting as multidrug resistance proteins (like the MDR1-P glycoprotein, or the multidrug resistance protein, MRP 1). So far, 48 ABC transporters, grouped into 7 families based on their sequence identity and function, have been identified.

[0004] ABC transporters provide protection against harmful environmental compounds by regulating a variety of important physiological roles within the body, and therefore represent important potential drug targets for the treatment of diseases associated with transporter defects, outwards cell drug transport, and other diseases in which modulation of ABC transporter activity may be beneficial.

[0005] The cAMP/ATP-mediated anion channel, CFTR, is one member of the ABC transporter family commonly associated with diseases, which is expressed in a variety of cell types, including absorptive and secretory epithelia cells, where it regulates anion flux across the membrane, as well as the activity of other ion channels and proteins. The activity of CFTR in epithelial cells is essential for the maintenance of electrolyte transport throughout the body, including respiratory and digestive tissue (Quinton, P.M., 1990. Cystic fibrosis: a disease in electrolyte transport. FASEB J. 4, 2709–2717).

[0006] The gene encoding CFTR has been identified and sequenced (Kerem, B., Rommens, J.M., Buchanan, J.A., Markiewicz, D., Cox, T.K., Chakravarti, A., Buchwald, M., Tsui, L.C., 1989. Identification of the cystic fibrosis gene: genetic analysis. Science 245, 1073–1080). CFTR comprises about 1480 amino acids that encode a protein made up of a tandem repeat of transmembrane domains, each containing six transmembrane helices and a nucleotide binding domain. The pair of transmembrane domains is linked by a large, polar, regulatory (R)-domain with multiple phosphorylation sites that regulate channel activity and cellular trafficking.

[0007] Cystic fibrosis is (CF) caused by a defect in this gene which induces mutations in CFTR. Cystic fibrosis is the most common fatal genetic disease in humans and affects ~0.04% of white individuals (Bobadilla, J.L., Macek, M., Jr, Fine, J.P., Farrell, P.M., 2002. Cystic fibrosis: a worldwide analysis of CFTR mutations--correlation with incidence data and application to screening. Hum. Mutat. 19, 575–606. doi:10.1002/humu.10041), for example, in the United States, about one in every 2,500 infants is affected, and up to 10 million people carry a single copy of the defective gene without apparent ill effects; moreover subjects bearing a single copy of the gene exhibit increased resistance to cholera and to dehydration resulting from diarrhea. This effect might explain the relatively high frequency of the CF gene within the population.

[0008] In contrast, individuals with two copies of the CF associated gene suffer from the debilitating and fatal effects of CF, including chronic lung infections.

[0009] In cystic fibrosis patients, mutations in endogenous respiratory epithelial CFTR fail to confer chloride and bicarbonate permeability to epithelial cells in lung and other tissues, thus leading to reduced apical anion secretion and disruptions of the ion and fluid transport. This decrease in anion transport causes an enhanced mucus and pathogenic agent accumulation in the lung triggering microbial infections that ultimately cause death in CF patients.

[0010] Beyond respiratory disease, CF patients also suffer from gastrointestinal problems and pancreatic insufficiency that result in death if left untreated. Furthermore, female subjects with cystic fibrosis suffer from decreased fertility, whilst males with cystic fibrosis are infertile.

[0011] A variety of disease causing mutations have been identified through sequence analysis of the CFTR gene of CF chromosomes (Kerem, B., Rommens, J.M., Buchanan, J.A., Markiewicz, D., Cox, T.K., Chakravarti, A., Buchwald, M., Tsui, L.C., 1989. Identification of the cystic fibrosis gene: genetic analysis. Science 245, 1073–1080). ΔF508-CFTR, the most common CF mutation (present in at least 1 allele in ~90% of CF patients) and occurring in approximately 70% of the cases of cystic fibrosis, contains a single amino acid deletion of phenylalanine 508. This deletion prevents the nascent protein from folding correctly, which protein in turn cannot exit the endoplasmic reticulum (ER) and traffic to the plasma membrane, and then is rapidly degraded. As a result, the number of channels present in the membrane is far less than in cells expressing wild-type CFTR. In addition to impaired trafficking, the mutation results in defective channel gating. Indeed, even if ΔF508-CFTR is allowed to reach the cell plasma membrane by low-temperature (27 °C) rescue where it can function as a cAMP-activated chloride channel, its activity is decreased significantly compared with WT-CFTR (Pasyk, E.A., Foskett, J.K., 1995. Mutant (ΔF508) Cystic Fibrosis Transmembrane Conductance Regulator Cl^- Channel Is Functional When Retained in Endoplasmic Reticulum of Mammalian Cells. J. Biol. Chem. 270, 12347–12350).

[0012] Other mutations with lower incidence have also been identified that alter the channel regulation or the channel conductance. In case of the channel regulation mutants, the mutated protein is properly trafficked and localized to the plasma membrane but either cannot be activated or cannot function as a chloride channel (e.g. missense mutations located within the nucleotide binding domains), examples of these mutations are G551D, G178R, and G1349D. Mutations affecting chloride conductance have a CFTR protein that is correctly trafficked to the cell membrane but that generates reduced chloride flow (e.g. missense mutations located within the membrane-spanning domain), examples of these mutations are R117H and R334W.

[0013] In addition to cystic fibrosis, CFTR activity modulation may be beneficial for other diseases not directly caused by mutations in CFTR, such as, for example, chronic obstructive pulmonary disease (COPD), dry eye disease, and Sjogren's syndrome.

[0014] COPD is characterized by a progressive and non-reversible airflow limitation, which is due to mucus hypersecretion, bronchiolitis, and emphysema. A potential treatment of mucus hypersecretion and impaired mucociliary clearance that is common in COPD could consist in using activators of mutant or wild-type CFTR. In particular, the anion secretion increase across CFTR may facilitate fluid transport into the airway surface liquid to hydrate the mucus and optimize periciliary fluid viscosity. The resulting enhanced mucociliary clearance would help in reducing the symptoms associated with COPD.

[0015] Dry eye disease is characterized by a decrease in tear production and abnormal tear film lipid, protein and mucin profiles. Many factors may cause dry eye disease, some of which include age, arthritis, LASIK eye surgery, chemical/thermal burns, medications, allergies, and diseases, such as cystic fibrosis and Sjogrens's syndrome. Increasing anion secretion via CFTR could enhance fluid transport from the corneal endothelial cells and secretory glands surrounding the eye, and eventually improve corneal hydration, thus helping to alleviate dry eye disease associated symptoms. Sjogrens's syndrome is an autoimmune disease where the immune system harms moisture-producing glands throughout the body, including the eye, mouth, skin, respiratory tissue, liver, vagina, and gut. The ensuing symptoms, include, dry eye, mouth, and vagina, as well as lung disease. Sjogrens's syndrome is also associated with rheumatoid arthritis, systemic lupus, systemic sclerosis, and polymyositis/dermatomyositis. The cause of the disease is believed to lie in defective protein trafficking, for which treatment options are limited. As a consequence, modulation of CFTR activity may help hydrate the various organs and help alleviate the associated symptoms.

[0016] In addition to CF, the defective protein trafficking induced by the ΔF508-CFTR has been shown to be the underlying basis for a wide range of other diseases, in particular diseases where the defective functioning of the endoplasmic reticulum (ER) may either prevent the CFTR protein to exit the cell, and/or the misfolded protein is degraded (Morello, J.-P., Bouvier, M., Petäjä-Repo, U.E., Bichet, D.G., 2000. Pharmacological chaperones: a new twist on receptor folding. Trends Pharmacol. Sci. 21, 466–469. doi:10.1016/S0165-6147(00)01575-3; Shastry, B.S., 2003. Neurodegenerative disorders of protein aggregation. Neurochem. Int. 43, 1–7. doi:10.1016/S0197-0186(02)00196-1; Zhang, W., Fujii, N., Naren, A.P., 2012. Recent advances and new perspectives in targeting CFTR for therapy of cystic fibrosis and enterotoxin-induced secretory diarrheas. Future Med. Chem. 4, 329–345. doi:10.4155/fmc.12.1).

[0017] A number of genetic diseases are associated with a defective ER processing equivalent to the defect observed with CFTR in CF such as glycanosis CDG type 1, hereditary emphysema (α-l-antitrypsin (PiZ variant)), congenital hyperthyroidism, osteogenesis imperfecta (Type I, II, or IV procollagen), hereditary hypofibrinogenemia (fibrinogen), ACT deficiency (α-l-antichymotrypsin), diabetes insipidus (DI), neurophyseal DI (vasopvessin hormoneN2-receptor), neprogenic DI (aquaporin II), Charcot-Marie Tooth syndrome (peripheral myelin protein 22), Perlizaeus-Merzbacher disease, neurodegenerative diseases such as Alzheimer's disease (APP and presenilins), Parkinson's disease, amyotrophic lateral sclerosis, progressive supranuclear palsy, Pick's disease, several polyglutamine neurological disorders such as Huntington's disease, spinocerebullar ataxia type I, spinal and bulbar muscular atrophy, dentatorubal pallidoluysian, and myotonic dystrophy, as well as spongiform encephalopathies, such as hereditary Creutzfeldt-Jakob disease (prion protein processing defect), Fabry disease (lysosomal α-galactosidase A), Straussler-Scheinker syndrome, chronic obstructive pulmonary disease (COPD), dry eye disease, and Sjogren's Syndrome.

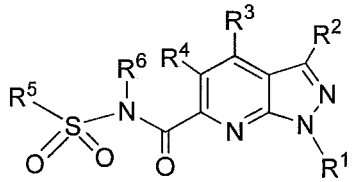
[0018] In addition to up-regulation of the activity of CFTR, anion secretion reduction by CFTR modulators may be beneficial for the treatment of secretory diarrheas, in which epithelial water transport is dramatically increased as a result of secretagogue activated chloride transport. The mechanism involves elevation of cAMP and stimulation of CFTR.

[0019] Regardless of the cause, excessive chloride transport is seen in all diarrhoeas, and results in dehydration, acidosis, impaired growth and death. Acute and chronic diarrhoeas remain a major medical problem worldwide, and are a significant factor in malnutrition, leading to death in children of less than five years old (5,000,000 deaths/year). Furthermore, in patients with chronic inflammatory bowel disease (IBD) and/or acquired immunodeficiency syndrome (AIDS), diarrhoea is a dangerous condition.

[0020] Accordingly, there is a need for novel compounds able to modulate CFTR. In particular, the present invention discloses compounds that may act as CFTR modulators for the treatment of cystic fibrosis. The present invention also provides methods for the preparation of these compounds, pharmaceutical compositions comprising these compounds and methods for the treatment of cystic fibrosis by administering the compounds of the invention.

SUMMARY

[0021] In one aspect thereis provided a compound of formula (I)



(I)

or a pharmaceutically acceptable salt thereof, wherein

R^1 is G^{1A}, C_1-C_6 haloalkyl, or C_1-C_6 alkyl; wherein the C_1-C_6 haloalkyl and the C_1-C_6 alkyl are each optionally substituted with one G^{1A};

G^{1A}, at each occurrence, is independently phenyl, 5-6 membered monocyclic heteroaryl, 4-7 membered monocyclic heterocycle, 5-11 membered fused bicyclic heterocycle, or C_3-C_6 monocyclic cycloalkyl; wherein each G^{1A} is optionally substituted with 1, 2, 3, or 4 substituents independently selected from the group consisting of R^{1a} and G^{1B};

G^{1B}, at each occurrence, is independently 4-7 membered monocyclic heterocycle which is optionally substituted with 1, 2, 3, or 4 independently selected R^{1b} groups;

R^2 is hydrogen, C_2-C_4 alkenyl, C_1-C_6 alkyl, C_1-C_6 haloalkyl, $-OR^{2xa}$, $-N(R^{2xa})(R^{2xb})$, or G^{2A};

R^{2xa}, at each occurrence, is independently C_1-C_6 alkyl, C_1-C_6 haloalkyl, or G^{2B};

R^{2xb} is hydrogen, C_1-C_3 alkyl, or C_1-C_3 haloalkyl;

G^{2A} and G^{2B} are each independently a 4-7 membered monocyclic heterocycle or a C_3-C_6 monocyclic cycloalkyl; wherein G^{2A} and G^{2B} are each optionally substituted with 1, 2, or 3 independently selected R^{2a} groups;

R^3 is G^{3A}, $-G^{3B}$-L^1-G^{3C}, $-G^{3B}$-L^3-G^{3C}-G^{3E}, -(C_1-C_6 alkylenyl)-G^{3D}, $-OR^{3a}$, or $-N(R^{3a})(R^{3b})$;

R^{3a}, at each occurrence, is independently G^{3D}, C_1-C_6 haloalkyl, or C_1-C_6 alkyl; wherein the C_1-C_6 haloalkyl and the C_1-C_6 alkyl are each optionally substituted with one or two substituents independently selected from the group consisting of G^{3D}, $-OR^{3xa}$, and $-N(R^{3xb})_2$;

R^{3xa} and R^{3xb}, at each occurrence, are each independently hydrogen, C_1-C_6 haloalkyl, C_1-C_6 alkyl, or G^{3D};

R^{3b} is hydrogen, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

L^1 is a bond, C_1-C_6 alkylenyl, (C_1-C_6 alkylenyl)$_r$-L^2-(C_1-C_6 alkylenyl)$_s$, or O-(C_1-C_6 alkylenyl)-C(O), wherein the left end of the L^1 moiety is attached to G^{3B};

L^2 is O, N(R^x), C(O), N(R^x)C(O), or C(O)N(R^x); wherein each R^x is independently hydrogen, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

L^3 is a bond or C_1-C_6 alkylenyl;

r is 0 or 1;

s is 0 or 1;

G^{3A}, G^{3B}, and G^{3C} and each independently C_3-C_{11} cycloalkyl, phenyl, 5-6 membered monocyclic heteroaryl, or 4-11 membered heterocycle; wherein G^{3A}, G^{3B}, and G^{3C} are each optionally substituted with 1, 2, 3, or 4 independently selected R^e groups;

G^{3D}, at each occurrence, is independently C_3-C_8 monocyclic cycloalkyl, 4-7 membered monocyclic heterocycle, a 5-11 membered fused bicyclic heterocycle, or a 5-11 membered spiro heterocycle; wherein each G^{3D} is optionally substituted with 1, 2, 3, or 4 substituents independently selected from the group consisting of R^e and G^{3E};

G^{3E}, at each occurrence, is independently C_3-C_8 monocyclic cycloalkyl or 4-7 membered monocyclic heterocycle; wherein each G^{3E} is optionally substituted with 1, 2, 3, or 4 independently selected R^e groups;

R^4 is hydrogen, C_1-C_3 alkyl, or C_1-C_3 haloalkyl;

R^5 is C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, -N(R^{5ax})(R^{5bx}), -OR^{5dx}, or G^{5A}; wherein the C_1-C_6 alkyl and the C_1-C_6 haloalkyl are each optionally substituted with one or two substituents independently selected from the group consisting of G^{5A}, -CN, -N_3, -OR^{5ax}, -$S(O)_2R^{5ax}$, -$S(O)_2N(R^{5ax})(R^{5bx})$, -N($R^{5ax}$)($R^{5bx}$), -N($R^{5bx}$)$S(O)_2R^{5cx}$, -N($R^{5bx}$)C(O)$R^{5cx}$, -N($R^{5bx}$)C(O)N($R^{5ax}$)($R^{5bx}$), -N($R^{5bx}$)C(O)$OR^{5cx}$, -C(O)$R^{5ax}$, -C(O)$OR^{5ax}$, -C(O)N($R^{5bx}$)$S(O)_2R^{5cx}$, and -C(O)N($R^{5ax}$)($R^{5bx}$);

R^{5ax} and R^{5bx}, at each occurrence, are each independently hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, -OR^{5ex}, -(C_1-C_6 alkylenyl)-OR^{5ex}, G^{5A}, or -(C_1-C_6 alkylenyl)-G^{5A};

R^{5cx}, at each occurrence, is independently C_1-C_6 alkyl, C_1-C_6 haloalkyl, G^{5A}, or -(C_1-C_6 alkylenyl)-G^{5A};

R^{5dx} is C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

R^{5ex} is hydrogen, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

G^{5A}, at each occurrence, is independently C_3-C_{11} cycloalkyl, phenyl, 5-6 membered monocyclic heteroaryl, or 4-11 membered heterocycle; wherein each G^{5A} is optionally substituted with 1, 2, 3, or 4 independently selected R^{5a} groups;

R^{5a}, at each occurrence, is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, C_1-C_6 haloalkyl, oxo, G^{5B}, -CN, NO_2, $-OR^b$, $-OC(O)R^c$, $-OC(O)N(R^d)_2$, $-SR^b$, $-S(O)_2R^b$, $-S(O)_2N(R^d)_2$, $-C(O)R^b$, $-C(O)OR^b$, $-C(O)N(R^d)_2$, $-C(O)N(R^d)S(O)_2R^c$, $-N(R^d)_2$, $-N(R^d)C(O)R^c$, $-N(R^d)S(O)_2R^c$, $-N(R^d)C(O)O(R^b)$, $-N(R^d)C(O)N(R^d)_2$, $-N(R^d)S(O)_2N(R^d)_2$, -(C_1-C_6 alkylenyl)-CN, -(C_1-C_6 alkylenyl)-G^{5B}, -(C_1-C_6 alkylenyl)-OR^b, -(C_1-C_6 alkylenyl)-$OC(O)R^c$, -(C_1-C_6 alkylenyl)-$OC(O)N(R^d)_2$, -(C_1-C_6 alkylenyl)-SR^b, -(C_1-C_6 alkylenyl)-$S(O)_2R^b$, -(C_1-C_6 alkylenyl)-$S(O)_2N(R^d)_2$, -(C_1-C_6 alkylenyl)-$C(O)R^b$, -(C_1-C_6 alkylenyl)-$C(O)OR^b$, -(C_1-C_6 alkylenyl)-$C(O)N(R^d)_2$, -(C_1-C_6 alkylenyl)-$C(O)N(R^d)S(O)_2R^c$, -(C_1-C_6 alkylenyl)-$N(R^d)_2$, -(C_1-C_6 alkylenyl)-$N(R^d)C(O)R^c$, -(C_1-C_6 alkylenyl)-$N(R^d)S(O)_2R^c$, -(C_1-C_6 alkylenyl)-$N(R^d)C(O)O(R^c)$, -(C_1-C_6 alkylenyl)-$N(R^d)C(O)N(R^d)_2$, or -(C_1-C_6 alkylenyl)-$N(R^d)S(O)_2N(R^d)_2$;

R^b and R^d, at each occurrence, are each independently hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, alkoxyalkyl, G^{5B}, or -(C_1-C_6 alkylenyl)-G^{5B};

R^c, at each occurrence, is independently C_1-C_6 alkyl, C_1-C_6 haloalkyl, alkoxyalkyl, G^{5B}, or -(C_1-C_6 alkylenyl)-G^{5B};

G^{5B}, at each occurrence, is independently C_3-C_6 monocyclic cycloalkyl, phenyl, 5-6 membered monocyclic heteroaryl, or 4-7 membered monocyclic heterocycle; wherein each G^{5B} is optionally substituted with 1, 2, 3, or 4 independently selected R^{5b} groups;

R^e, at each occurrence, is independently C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 alkyl, C_1-C_6 haloalkyl, halogen, oxo, -CN, $-N_3$, NO_2, $-OR^f$, $-OC(O)R^g$, $-OC(O)NR^fR^h$, $-SR^f$, $-S(O)_2R^f$, $-S(O)_2NR^fR^h$, $-C(O)R^f$, $-C(O)OR^f$, $-C(O)NR^fR^h$, $-C(O)N(R^h)S(O)_2R^f$, $-N(R^f)_2$, $-N(R^h)C(O)R^h$, $-N(R^h)S(O)_2R^g$, $-N(R^h)C(O)O(R^g)$, $-N(R^h)C(O)NR^fR^h$, or $-N(R^h)S(O)_2NR^fR^h$; wherein the C_1-C_6 haloalkyl and the C_1-C_6 alkyl are each optionally substituted with 1 or 2 substituents independently selected from the group consisting of -CN, NO_2, $-OR^f$, $-OC(O)R^g$, $-OC(O)NR^fR^h$, $-SR^f$, $-S(O)_2R^f$,

$-S(O)_2NR^fR^h$, $-C(O)R^f$, $-C(O)OR^f$, $-C(O)NR^fR^h$, $-C(O)N(R^h)S(O)_2R^f$, $-N(R^f)_2$, $-N(R^h)C(O)R^g$, $-N(R^h)S(O)_2R^g$, $-N(R^h)C(O)O(R^g)$, $-N(R^h)C(O)NR^fR^h$, and $-N(R^h)S(O)_2NR^fR^h$;

R^f, at each occurrence, is independently hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, -(C_1-C_6 alkylenyl)-CN, -(C_1-C_6 alkylenyl)-OR^m, -(C_1-C_6 alkylenyl)-$OC(O)R^n$, -(C_1-C_6 alkylenyl)-$OC(O)N(R^m)_2$, -(C_1-C_6 alkylenyl)-SR^m, -(C_1-C_6 alkylenyl)-$S(O)_2R^m$, -(C_1-C_6 alkylenyl)-$S(O)_2N(R^m)_2$, -(C_1-C_6 alkylenyl)-$C(O)R^m$, -(C_1-C_6 alkylenyl)-$C(O)OR^m$, -(C_1-C_6 alkylenyl)-$C(O)N(R^m)_2$, -(C_1-C_6 alkylenyl)-$C(O)N(R^m)S(O)_2R^n$, -(C_1-C_6 alkylenyl)-$N(R^m)_2$, -(C_1-C_6 alkylenyl)-$N(R^m)C(O)R^n$, -(C_1-C_6 alkylenyl)-$N(R^m)S(O)_2R^n$, -(C_1-C_6 alkylenyl)-$N(R^m)C(O)O(R^n)$, -(C_1-C_6 alkylenyl)-$N(R^m)C(O)N(R^m)_2$, or -(C_1-C_6 alkylenyl)-$N(R^m)S(O)_2N(R^m)_2$;

R^g, at each occurrence, is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, -(C_1-C_6 alkylenyl)-CN, -(C_1-C_6 alkylenyl)-OR^m, -(C_1-C_6 alkylenyl)-$OC(O)R^n$, -(C_1-C_6 alkylenyl)-$OC(O)N(R^m)_2$, -(C_1-C_6 alkylenyl)-SR^m, -(C_1-C_6 alkylenyl)-$S(O)_2R^m$, -(C_1-C_6 alkylenyl)-$S(O)_2N(R^m)_2$, -(C_1-C_6 alkylenyl)-$C(O)R^m$, -(C_1-C_6 alkylenyl)-$C(O)OR^m$, -(C_1-C_6 alkylenyl)-$C(O)N(R^m)_2$, -(C_1-C_6 alkylenyl)-$C(O)N(R^m)S(O)_2R^n$, -(C_1-C_6 alkylenyl)-$N(R^m)_2$, -(C_1-C_6 alkylenyl)-$N(R^m)C(O)R^n$, -(C_1-C_6 alkylenyl)-$N(R^m)S(O)_2R^n$, -(C_1-C_6 alkylenyl)-$N(R^m)C(O)O(R^n)$, -(C_1-C_6 alkylenyl)-$N(R^m)C(O)N(R^m)_2$, or -(C_1-C_6 alkylenyl)-$N(R^m)S(O)_2N(R^m)_2$;

R^h, at each occurrence, is independently hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, or -(C_1-C_6 alkylenyl)-OR^m;

R^{1a}, R^{1b}, R^{2a}, and R^{5b}, at each occurrence, are each independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, C_1-C_6 haloalkyl, oxo, -CN, $-NO_2$, $-OR^m$, $-OC(O)R^n$, $-OC(O)N(R^m)_2$, $-SR^m$, $-S(O)_2R^m$, $-S(O)_2N(R^m)_2$, $-C(O)R^m$, $-C(O)OR^m$, -C(O)O(benzyl), $-C(O)N(R^m)_2$, $-C(O)N(R^m)S(O)_2R^n$, $-N(R^m)_2$, $-N(R^m)$(alkoxyalkyl), $-N$(alkoxyalkyl)$_2$, $-N(R^m)C(O)R^n$, $-N(R^m)S(O)_2R^n$, $-N(R^m)C(O)O(R^n)$, $-N(R^m)C(O)N(R^m)_2$, $-N(R^m)S(O)_2N(R^m)_2$, -(C_1-C_6 alkylenyl)-CN, -(C_1-C_6 alkylenyl)-OR^m, -(C_1-C_6 alkylenyl)-$OC(O)R^n$, -(C_1-C_6 alkylenyl)-$OC(O)N(R^m)_2$, -(C_1-C_6 alkylenyl)-SR^m, -(C_1-C_6 alkylenyl)-$S(O)_2R^m$, -(C_1-C_6 alkylenyl)-$S(O)_2N(R^m)_2$, -(C_1-C_6 alkylenyl)-$C(O)R^m$, -(C_1-C_6 alkylenyl)-

$C(O)OR^m$, -(C_1-C_6 alkylenyl)-$C(O)N(R^m)_2$, -(C_1-C_6 alkylenyl)-$C(O)N(R^m)S(O)_2R^n$, -(C_1-C_6 alkylenyl)-$N(R^m)_2$, -(C_1-C_6 alkylenyl)-$N(R^m)C(O)R^n$, -(C_1-C_6 alkylenyl)-$N(R^m)S(O)_2R^n$, -(C_1-C_6 alkylenyl)-$N(R^m)C(O)O(R^n)$, -(C_1-C_6 alkylenyl)-$N(R^m)C(O)N(R^n)_2$, or -(C_1-C_6 alkylenyl)-$N(R^m)S(O)_2N(R^n)_2$;

R^m, at each occurrence, is independently hydrogen, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

R^n, at each occurrence, is independently C_1-C_6 alkyl or C_1-C_6 haloalkyl;

R^6 is hydrogen, C_1-C_6 alkyl, or C_1-C_6 haloalkyl; or

R^5 and R^6 together form a C_1-C_6 alkylenyl or -$N(R^z)$-(C_1-C_6 alkylenyl)- wherein the $N(R^z)$ is attached to the $S(O)_2$ moiety of formula (I); and

R^z is hydrogen, C_1-C_6 alkyl, or C_1-C_6 haloalkyl.

[0021a] In another aspect, there is provided benzyl 3-({3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)pyrrolidine-1-carboxylate, or a pharmaceutically acceptable salt thereof.

[0021b] In another aspect, there is provided 3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[2-(methoxymethyl)morpholin-4-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide, or a pharmaceutically acceptable salt thereof.

[0021c] In another aspect, there is provided 3-cyclobutyl-*N*-(morpholine-4-sulfonyl)-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide, or a pharmaceutically acceptable salt thereof.

[0021d] In another aspect, there is provided 3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide, or a pharmaceutically acceptable salt thereof.

[0021e] In another aspect, there is provided 3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[4-(propan-2-yl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide, or a pharmaceutically acceptable salt thereof.

[0021f] In another aspect, there is provided 3-cyclobutyl-N-(morpholine-4-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxamide, or a pharmaceutically acceptable salt thereof.

[0021g] In another aspect, there is provided 3-cyclobutyl-N-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-(2-methoxypyridin-4-yl)-1H-pyrazolo[3,4-b]pyridine-6-carboxamide, or a pharmaceutically acceptable salt thereof.

[0021h] In another aspect, there is provided N-(2-acetamidoethanesulfonyl)-3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxamide, or a pharmaceutically acceptable salt thereof.

[0022] Another embodiment of the disclosure relates to pharmaceutical compositions comprising a compound of the dislosure, and a pharmaceutical carrier. In another aspect, there is provided a pharmaceutical composition comprising a therapeutically effective amount of a compound as disclosed herein, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier. Such compositions can be administered in accordance with a method of thedisclosure, typically as part of a therapeutic regimen for treatment or prevention of conditions and disorders related to Cystic Fibrosis Transmembrane Conductance Regulator activity. In a particular embodiment, the pharmaceutical compositions may additionally comprise further therapeutically active ingredients suitable for use in combination with the compounds of the disclosure. In another aspect, there is provided a pharmaceutical composition comprising a compound as described herein or a pharmaceutically acceptable salt thereof, and one or more additional therapeutic agents. In another aspect, there is provided a pharmaceutical composition comprising a compound as described herein or a pharmaceutically acceptable salt thereof, one potentiator, and one or more additional correctors. In a more particular embodiment, the further therapeutically active ingredient is an agent for the treatment of cystic fibrosis.

[0023] Moreover, the compounds of the disclosure, useful in the pharmaceutical compositions and treatment methods disclosed herein, are pharmaceutically acceptable as prepared and used.

[0024] Yet another embodiment of the disclosure relates to a method for treating, or preventing conditions and disorders related to Cystic Fibrosis Transmembrane Conductance Regulator activity in mammals. More particularly, the method is useful for treating or preventing conditions and disorders related to cystic fibrosis, Sjögren's syndrome, pancreatic insufficiency, chronic obstructive lung disease, or chronic obstructive airway disease. Accordingly, the compounds and compositions of the disclosure are useful as a medicament for treating or preventing Cystic Fibrosis Transmembrane Conductance Regulator modulated disease.

[0025] The compounds, compositions comprising the compounds, methods for making the compounds, and methods for treating or preventing conditions and disorders by administering the compounds are further described herein.

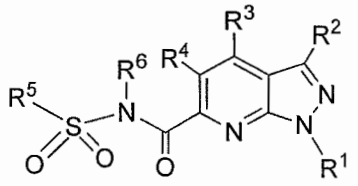
[0026] In a particular embodiment, the compounds of the disclosure are provided for use in the treatment of cystic fibrosis. In a particular embodiment, the compounds of the disclosure are provided for use in the treatment of cystic fibrosis caused by class I, II, III, IV, V, and/or VI mutations. In another aspect, there is provided use of a compound as disclosed herein or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cystic fibrosis in a subject in need thereof. In another aspect, there is provided use of a compound as described herein or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cystic fibrosis in a subject in need thereof, wherein the medicament is to be administered with one potentiator, and one or more additional correctors. In another aspect, there is provided use of a compound as described herein or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating cystic fibrosis in a subject in need thereof, wherein the medicament is to be admininstered with one or more additional therapeutic agents.

[0027] The present disclosure also provides pharmaceutical compositions comprising a compound of the disclosure, and a suitable pharmaceutical carrier for use in medicine. In another aspect, there is provided a compound as disclosed herein or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as disclosed herein, for use in medicine. In a particular embodiment, the pharmaceutical composition is for use in the treatment of cystic fibrosis. In another aspect, there is provided a compound as disclosed herein or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition as disclosed herein, for use in the treatment of cystic fibrosis.

[0028] These and other objects of the disclosure are described in the following paragraphs. These objects should not be deemed to narrow the scope of the disclosure.

DETAILED DESCRIPTION OF THE INVENTION

[0029] Described herein are compounds of formula (I)



(I)

wherein R^1, R^2, R^3, R^4, R^5, and R^6, are defined above in the Summary of the Invention and below in the Detailed Description. Further, compositions comprising such compounds and methods for treating conditions and disorders using such compounds and compositions are also described.

[0030] Compounds included herein may contain one or more variable(s) that occur more than one time in any substituent or in the formulae herein. Definition of a variable on each occurrence is independent of its definition at another occurrence. Further, combinations of substituents are permissible only if such combinations result in stable compounds. Stable compounds are compounds, which can be isolated from a reaction mixture.

Definitions

[0031] It is noted that, as used in this specification and the intended claims, the singular form "a," "an," and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "a compound" includes a single compound as well as one or more of the same or different compounds; reference to "a pharmaceutically acceptable carrier" means a single pharmaceutically acceptable carrier as well as one or more pharmaceutically acceptable carriers, and the like.

[0032] As used in the specification and the appended claims, unless specified to the contrary, the following terms have the meaning indicated:

[0033] The term "alkenyl" as used herein, means a straight or branched hydrocarbon chain containing from 2 to 10 carbons and containing at least one carbon-carbon double bond. The term "C_2-C_6 alkenyl" means an alkenyl group containing 2-6 carbon atoms. Non-limiting examples of C_2-C_6 alkenyl include buta-1,3-dienyl, ethenyl, 2-propenyl, 2-methyl-2-propenyl, 3-butenyl, 4-pentenyl, and 5-hexenyl.

[0034] The term "alkoxy" as used herein, means a C_1-C_6 alkyl group, as defined herein, appended to the parent molecular moiety through an oxygen atom. Non-limiting examples of alkoxy include methoxy, ethoxy, propoxy, 2-propoxy, butoxy, *tert*-butoxy, pentyloxy, and hexyloxy.

[0035] The term "alkoxyalkyl" as used herein, means an alkoxy group, as defined herein, appended to the parent molecular moiety through a C_1-C_6 alkyl group, as defined herein. Non-limiting examples of alkoxyalkyl include *tert*-butoxymethyl, 2-ethoxyethyl, 2-methoxyethyl, and methoxymethyl.

[0036] The term "alkyl" as used herein, means a saturated, straight or branched hydrocarbon chain radical. In some instances, the number of carbon atoms in an alkyl moiety is indicated by the prefix "C_x-C_y", wherein x is the minimum and y is the maximum number of carbon atoms in the substituent. Thus, for example, "C_1-C_6 alkyl" means an alkyl substituent containing from 1 to 6 carbon atoms and "C_1-C_3 alkyl" means an alkyl substituent containing from 1 to 3 carbon atoms. Representative examples of alkyl include, but are not limited to, methyl, ethyl, *n*-propyl, iso-propyl, *n*-butyl, *sec*-butyl, iso-butyl, *tert*-butyl, *n*-pentyl, isopentyl, neopentyl, *n*-hexyl, 1-methylbutyl, 2-methylbutyl, 3-methylbutyl, 3,3-dimethylbutyl, 1,1-dimethylpropyl, 1,2-dimethylpropyl, 2,2-dimethylpropyl, 1-methylpropyl, 2-methylpropyl, 1-ethylpropyl, and 1,2,2-trimethylpropyl. The terms "alkyl," "C_1-C_6 alkyl," "C_1-C_4 alkyl," and "C_1-C_3 alkyl" used herein are unsubstituted, unless otherwise indicated.

[0037] The term "alkylene" or "alkylenyl" means a divalent radical derived from a straight or branched, saturated hydrocarbon chain, for example, of 1 to 10 carbon atoms or of 1 to 6 carbon atoms (C_1-C_6 alkylenyl) or of 1 to 4 carbon atoms or of 1 to 3 carbon atoms (C_1-C_3 alkylenyl) or of 2 to 6 carbon atoms (C_2-C_6 alkylenyl). Examples of C_1-C_6 alkylenyl include, but

are not limited to, -CH_2-, -CH_2CH_2-, -$C(CH_3)_2$-$CH_2CH_2CH_2$-, -$C(CH_3)_2$-CH_2CH_2-, -$CH_2CH_2CH_2CH_2$-, and -$CH_2CH(CH_3)CH_2$-.

[0038] The term "C_2-C_6 alkynyl" as used herein, means a straight or branched chain hydrocarbon radical containing from 2 to 6 carbon atoms and containing at least one carbon-carbon triple bond. Representative examples of C_2-C_6 alkynyl include, but are not limited, to acetylenyl, 1-propynyl, 2-propynyl, 3-butynyl, 2-pentynyl, and 1-butynyl.

[0039] The term "C_3-C_{11} cycloalkyl" as used herein, means a hydrocarbon ring radical containing 3-11 carbon atoms, zero heteroatom, and zero double bond. The C_3-C_{11} cycloalkyl group may be a single-ring (monocyclic) or have two or more rings (polycyclic or bicyclic). Monocyclic cycloalkyl groups typically contain from 3 to 8 carbon ring atoms (C_3-C_8 monocyclic cycloalkyl), and even more typically 3-6 carbon ring atoms (C_3-C_6 monocyclic cycloalkyl). Examples of monocyclic cycloalkyls include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl. Polycyclic cycloalkyl groups contain two or more rings, and bicyclic cycloalkyls contain two rings. In certain embodiments, the polycyclic cycloalkyl groups contain 2 or 3 rings. The rings within the polycyclic and the bicyclic cycloalkyl groups may be in a bridged, fused, or spiro orientation, or combinations thereof. In a spirocyclic cycloalkyl, one atom is common to two different rings. An example of a spirocyclic cycloalkyl is spiro[4.5]decane. In a bridged cycloalkyl, the rings share at least two non-adjacent atoms. Examples of bridged cycloalkyls include, but are not limited to, bicyclo[2.2.2]octyl, bicyclo[3.2.1]octyl, bicyclo[3.1.1]heptyl, bicyclo[2.2.1]heptyl, bicyclo[3.2.2]nonyl, bicyclo[3.3.1]nonyl, and bicyclo[4.2.1]nonyl, tricyclo[3.3.1.$0^{3,7}$]nonyl (octahydro-2,5-methanopentalenyl or noradamantyl), tricyclo[3.3.1.$1^{3,7}$]decyl (adamantyl), and tricyclo[4.3.1.$1^{3,8}$]undecyl (homoadamantyl). In a fused ring cycloalkyl, the rings share one common bond. Examples of fused-ring cycloalkyl include, but not limited to, decalin (decahydronaphthyl) and bicyclo[2.2.0]octyl.

[0040] The term "C_4-C_7 monocyclic cycloalkenyl" as used herein, means cyclobutenyl, cyclopentenyl, cyclohexenyl, and cycloheptyl.

[0041] The term "halo" or "halogen" as used herein, means Cl, Br, I, and F.

[0042] The term "haloalkyl" as used herein, means an alkyl group, as defined herein, in which one, two, three, four, five or six hydrogen atoms are replaced by halogen. The term "C_1-C_6 haloalkyl" means a C_1-C_6 alkyl group, as defined herein, in which one, two, three, four,

five, or six hydrogen atoms are replaced by halogen. The term "C_1-C_3 haloalkyl" means a C_1-C_3 alkyl group, as defined herein, in which one, two, three, four, or five hydrogen atoms are replaced by halogen. Representative examples of haloalkyl include, but are not limited to, chloromethyl, 2-fluoroethyl, 2,2-difluoroethyl, fluoromethyl, 2,2,2-trifluoroethyl, trifluoromethyl, difluoromethyl, pentafluoroethyl, 2-chloro-3-fluoropentyl, trifluorobutyl, and trifluoropropyl. The terms "haloalkyl," "C_1-C_6 haloalkyl," and "C_1-C_3 haloalkyl" used herein are unsubstituted, unless otherwise indicated.

[0043] The term "4-11 membered heterocycle" as used herein, means a hydrocarbon ring radical of 4-11 carbon ring atoms wherein at least one carbon atom is replaced by a heteroatom(s) independently selected from the group consisting of O, N, and S. The 4-11 membered heterocycle ring may be a single ring (monocyclic) or have two or more rings (bicyclic or polycyclic). In certain embodiments, the monocyclic heterocycle is a four-, five-, six-, seven-, or eight-membered hydrocarbon ring wherein at least one carbon ring atom is replaced by a heteroatom(s) independently selected from the group consisting of O, N, and S. In certain embodiments, the monocyclic heterocycle is a 4-7 membered hydrocarbon ring wherein at least one carbon ring atom is replaced by a heteroatom(s). A four-membered monocyclic heterocycle contains zero or one double bond, and one heteroatom selected from the group consisting of O, N, and S. A five-membered monocyclic heterocycle contains zero or one double bond and one, two, or three heteroatoms selected from the group consisting of O, N, and S. Examples of five-membered monocyclic heterocycles include those containing in the ring: 1 O; 1 S; 1 N; 2 N; 3 N; 1 S and 1 N; 1 S, and 2 N; 1 O and 1 N; or 1 O and 2 N. Non-limiting examples of 5-membered monocyclic heterocyclic groups include 1,3-dioxolanyl, tetrahydrofuranyl, dihydrofuranyl, tetrahydrothienyl, dihydrothienyl, imidazolidinyl, oxazolidinyl, imidazolinyl, imidazolidinyl, isoxazolidinyl, pyrazolidinyl, pyrazolinyl, pyrrolidinyl, 2-pyrrolinyl, 3-pyrrolinyl, thiazolinyl, and thiazolidinyl. A six-membered monocyclic heterocycle contains zero, one, or two double bonds and one, two, or three heteroatoms selected from the group consisting of O, N, and S. Examples of six-membered monocyclic heterocycles include those containing in the ring: 1 O; 2 O; 1 S; 2 S; 1 N; 2 N; 3 N; 1 S, 1 O, and 1 N; 1 S and 1 N; 1 S and 2 N; 1 S and 1 O; 1 S and 2 O; 1 O and 1 N; and 1 O and 2 N. Examples of six-membered monocyclic heterocycles include 1,6-dihydropyridazinyl, dihydropyranyl, 1,3-dioxanyl, 1,4-dithianyl, hexahydropyrimidine, morpholinyl, piperazinyl,

piperidinyl, tetrahydropyranyl, 1,2,3,6-tetrahydropyridinyl, tetrahydrothiopyranyl, thiomorpholinyl, thioxanyl, and trithianyl. Seven- and eight-membered monocyclic heterocycles contains zero, one, two, or three double bonds and one, two, or three heteroatoms selected from the group consisting of O, N, and S. Examples of monocyclic heterocycles include, but are not limited to, azetidinyl, azepanyl, aziridinyl, 1,4-diazepanyl, dihydropyranyl, 1,6-dihydropyridazinyl, 1,3-dioxanyl, 1,3-dioxolanyl, 1,3-dithiolanyl, 1,3-dithianyl, imidazolinyl, imidazolidinyl, isothiazolinyl, isothiazolidinyl, isoxazolinyl, isoxazolidinyl, morpholinyl, oxazepanyl, oxadiazolinyl, oxadiazolidinyl, oxazolinyl, oxazolidinyl, oxetanyl, piperazinyl, piperidinyl, pyranyl, pyrazolinyl, pyrazolidinyl, pyrrolinyl, pyrrolidinyl, tetrahydrofuranyl, tetrahydropyridinyl, tetrahydropyranyl, tetrahydrothienyl, thiadiazolinyl, thiadiazolidinyl, thiazolinyl, thiazolidinyl, thiomorpholinyl, thiopyranyl, and trithianyl. Polycyclic heterocycle groups contain two or more rings, and bicyclic heterocycles contain two rings. In certain embodiments, the polycyclic heterocycle groups contain 2 or 3 rings. The rings within the polycyclic and the bicyclic heterocycle groups may be in a bridged, fused, or spiro orientation, or combinations thereof. In a spirocyclic heterocycle, one atom is common to two different rings. Non-limiting examples of the spirocyclic heterocycle include 2-azaspiro[3.3]heptyl, 5-azaspiro[2.4]heptyl, 5-azaspiro[2.5]octyl, 2-azaspiro[3.5]nonyl, 2-azaspiro[3.4]octyl, 3-azaspiro[5.5]undecyl, 5-azaspiro[3.4]octyl, 2-oxaspiro[3.3]heptyl, 2-oxa-6-azaspiro[3.3]heptyl, 6-oxa-2-azaspiro[3.4]octyl, 6-azaspiro[3.4]octyl, 7-azaspiro[3.5]nonyl, 8-azaspiro[4.5]decyl, 1-oxa-7-azaspiro[4.4]nonyl, 1-oxa-7-azaspiro[3.5]nonyl, 1-oxa-8-azaspiro[4.5]decyl, 1-oxa-3,8-diazaspiro[4.5]decyl, 1-oxa-4,9-diazaspiro[5.5]undecyl, 3,9-diazaspiro[5.5]undecyl, 2-oxa-7-azaspiro[3.5]nonyl, 5-oxa-2-azaspiro[3.5]nonyl, 6-oxa-2-azaspiro[3.5]nonyl, 2-oxa-5,8-diazaspiro[3.5]nonyl, 7-oxa-2-azaspiro[3.5]nonyl, 8-oxa-1-azaspiro[4.5]decyl, 8-oxa-2-azaspiro[4.5]decyl, 2,7-diazaspiro[4.4]nonyl, 1,4-dioxa-8-azaspiro[4.5]decyl, 1,3,8-triazaspiro[4.5]decyl. In a fused ring heterocycle, the rings share one common bond. Examples of fused bicyclic heterocycles are a 4-6 membered monocyclic heterocycle fused to a phenyl group, or a 4-6 membered monocyclic heterocycle fused to a C_3-C_6 monocyclic cycloalkyl, or a 4-6 membered monocyclic heterocycle fused to a C_4-C_7 monocyclic cycloalkenyl, or a 4-6 membered monocyclic heterocycle fused to a 4-7 membered monocyclic heterocycle. Examples of fused bicyclic heterocycles include, but are not limited to, 1,3-benzodioxolyl, 3-azabicyclo[3.1.0]hexyl, benzopyranyl, benzothiopyranyl, indolinyl, decahydropyrrolo[3,4-

b]azepinyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl, 2,3-dihydro-1*H*-indolyl, 3,4-dihydroisoquinolin-2(1*H*)-yl, 2,3,4,6-tetrahydro-1*H*-pyrido[1,2-*a*]pyrazin-2-yl, hexahydropyrano[3,4-*b*][1,4]oxazin-1(5*H*)-yl, hexahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl, hexahydrocyclopenta[c]pyrrol-3a(1*H*)-yl, hexahydro-1*H*-oxazolo[3,4-*a*]pyrazinyl, octahydropyrrolo[3,4-*b*][1,4]oxazinyl, octahydroimidazo[1,5-*a*]pyrazinyl, octahydropyrrolo[1,2-*a*]pyrazinyl, octahydro-1*H*-pyrrolo[3,2-*c*]pyridinyl, and octahydropyrrolo[3,4-*c*]pyrrolyl. In a bridged heterocycle, the rings share at least two non-adjacent atoms. Examples of such bridged heterocycles include, but are not limited to, azabicyclo[2.2.1]heptyl (including 2-azabicyclo[2.2.1]hept-2-yl and 2-oxa-5-azabicyclo[2.2.1]heptyl), 8-azabicyclo[3.2.1]oct-8-yl, octahydro-2,5-epoxypentalene, 8-oxa-3-azabicyclo[3.2.1]octyl, hexahydro-1*H*-1,4-methanocyclopenta[*c*]furan, aza-admantane (1-azatricyclo[3.3.1.$1^{3,7}$]decane), and oxa-adamantane (2-oxatricyclo[3.3.1.$1^{3,7}$]decane). The nitrogen and sulfur heteroatoms in the heterocycle rings may optionally be oxidized (e.g. 1,1-dioxidotetrahydrothienyl, 1,1-dioxido-1,2-thiazolidinyl, 1,1-dioxidothiomorpholinyl) and the nitrogen atoms may optionally be quaternized.

[0044] The term "5-11 membered heteroaryl" as used herein, means a monocyclic heteroaryl and a bicyclic heteroaryl. The monocyclic heteroaryl is a five- or six-membered ring. The five-membered ring contains two double bonds. The five membered ring may contain one heteroatom selected from O or S; or one, two, three, or four nitrogen atoms and optionally one oxygen or one sulfur atom. The six-membered ring contains three double bonds and one, two, three or four nitrogen atoms. Examples of 5-6 membered monocyclic heteroaryl include, but are not limited to, furanyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, 1,3-oxazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, pyrazolyl, pyrrolyl, tetrazolyl, thiadiazolyl, 1,3-thiazolyl, thienyl, triazolyl, and triazinyl. The bicyclic heteroaryl consists of a monocyclic heteroaryl fused to a phenyl, or a monocyclic heteroaryl fused to a C_3-C_6 monocyclic cycloalkyl, or a monocyclic heteroaryl fused to C_4-C_7 monocyclic cycloalkenyl, or a monocyclic heteroaryl fused to a monocyclic heteroaryl, or a monocyclic heteroaryl fused to a 4-7 membered monocyclic heterocycle. Representative examples of bicyclic heteroaryl groups include, but are not limited to, benzofuranyl, benzothienyl, benzoxazolyl, benzimidazolyl, benzoxadiazolyl, phthalazinyl, 2,6-dihydropyrrolo[3,4-*c*]pyrazol-5(4*H*)-yl, 6,7-dihydro-pyrazolo[1,5-*a*]pyrazin-5(4*H*)-yl, 6,7-dihydro-1,3-benzothiazolyl, imidazo[1,2-*a*]pyridinyl, indazolyl, indolyl, isoindolyl,

isoquinolinyl, naphthyridinyl, pyridoimidazolyl, quinolinyl, 2,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridin-5-yl, thiazolo[5,4-*b*]pyridin-2-yl, thiazolo[5,4-*d*]pyrimidin-2-yl, and 5,6,7,8-tetrahydroquinolin-5-yl. The nitrogen atom in the heteroaryl rings may optionally be oxidized and may optionally be quaternized.

[0045] The phenyl, the cycloalkyls, the cycloalkenyls, the heterocycles, and the heteroaryls, including the exemplary rings, are optionally substituted unless otherwise indicated; and are attached to the parent molecular moiety through any substitutable atom contained within the ring system.

[0046] The term "heteroatom" as used herein, means a nitrogen, oxygen, and sulfur.

[0047] The term "oxo" as used herein, means a =O group.

[0048] The term "radiolabel" means a compound of the invention in which at least one of the atoms is a radioactive atom or a radioactive isotope, wherein the radioactive atom or isotope spontaneously emits gamma rays or energetic particles, for example alpha particles or beta particles, or positrons. Examples of such radioactive atoms include, but are not limited to, ^{3}H (tritium), ^{14}C, ^{11}C, ^{15}O, ^{18}F, ^{35}S, ^{123}I, and ^{125}I.

[0049] A moiety is described as "substituted" when a non-hydrogen radical is in the place of hydrogen radical of any substitutable atom of the moiety. Thus, for example, a substituted heterocycle moiety is a heterocycle moiety in which at least one non-hydrogen radical is in the place of a hydrogen radical on the heterocycle. It should be recognized that if there are more than one substitution on a moiety, each non-hydrogen radical may be identical or different (unless otherwise stated).

[0050] If a moiety is described as being "optionally substituted," the moiety may be either (1) not substituted or (2) substituted. If a moiety is described as being optionally substituted with up to a particular number of non-hydrogen radicals, then that moiety may be either (1) not substituted; or (2) substituted by up to that particular number of non-hydrogen radicals or by up to the maximum number of substitutable positions on the moiety, whichever is less. Thus, for example, if a moiety is described as a heteroaryl optionally substituted with up to 3 non-hydrogen radicals, then any heteroaryl with less than 3 substitutable positions would be optionally substituted by up to only as many non-hydrogen radicals as the heteroaryl has substitutable positions. To illustrate, tetrazolyl (which has only one substitutable position) would be optionally substituted with up to one non-hydrogen radical. To illustrate further, if an amino

nitrogen is described as being optionally substituted with up to 2 non-hydrogen radicals, then a primary amino nitrogen will be optionally substituted with up to 2 non-hydrogen radicals, whereas a secondary amino nitrogen will be optionally substituted with up to only 1 non-hydrogen radical.

[0051] The terms "treat", "treating", and "treatment" refer to a method of alleviating or abrogating a disease and/or its attendant symptoms. In certain embodiments, "treat," "treating," and "treatment" refer to ameliorating at least one physical parameter, which may not be discernible by the subject. In yet another embodiment, "treat", "treating", and "treatment" refer to modulating the disease or disorder, either physically (for example, stabilization of a discernible symptom), physiologically (for example, stabilization of a physical parameter), or both. In a further embodiment, "treat", "treating", and "treatment" refer to slowing the progression of the disease or disorder.

[0052] The terms "prevent", "preventing", and "prevention" refer to a method of preventing the onset of a disease and/or its attendant symptoms or barring a subject from acquiring a disease. As used herein, "prevent", "preventing" and "prevention" also include delaying the onset of a disease and/or its attendant symptoms and reducing a subject's risk of acquiring or developing a disease or disorder.

[0053] The phrase "therapeutically effective amount" means an amount of a compound, or a pharmaceutically acceptable salt thereof, sufficient to prevent the development of or to alleviate to some extent one or more of the symptoms of the condition or disorder being treated when administered alone or in conjunction with another therapeutic agent for treatment in a particular subject or subject population. The "therapeutically effective amount" may vary depending on the compound, the disease and its severity, and the age, weight, health, etc., of the subject to be treated. For example in a human or other mammal, a therapeutically effective amount may be determined experimentally in a laboratory or clinical setting, or may be the amount required by the guidelines of the United States Food and Drug Administration, or equivalent foreign agency, for the particular disease and subject being treated.

[0054] The term "subject" is defined herein to refer to animals such as mammals, including, but not limited to, primates (e.g., humans), cows, sheep, goats, pigs, horses, dogs, cats, rabbits, rats, mice and the like. In one embodiment, the subject is a human. The terms "human," "patient," and "subject" are used interchangeably herein.

[0055] The term 'one or more' refers to one to four. In one embodiment it refers to one or three. In another embodiment it refers to one to three. In a further embodiment it refers to one to two. In yet other embodiment it refers to two. In yet other further embodiment it refers to one.

[0056] As used herein, "Class I mutation(s)" refers to mutations which interfere with protein synthesis. They result in the introduction of a premature signal of termination of translation (stop codon) in the mRNA. The truncated CFTR proteins are unstable and rapidly degraded, so, the net effect is that there is no protein at the apical membrane. In particular, Class I mutation(s) refers to p.Gly542X (G542X), W1282X, c.489+1G>T (621+1G>T), or c.579+1G>T (711+1G>T) mutation. More particularly, Class I mutation(s) refers to G542X; or W1282X mutations.

[0057] As used herein, "Class II mutation(s)" refers to mutations which affect protein maturation. These lead to the production of a CFTR protein that cannot be correctly folded and/or trafficked to its site of function on the apical membrane. In particular, Class II mutation(s) refers to p.Phe508del (F508del), p.Ile507del, or p.Asn1303Lys (N1303K) mutations. More particularly, Class II mutation(s) refers to F508del or N1303K mutations.

[0058] As used herein, "Class III mutation(s)" refers to mutations which alter the regulation of the CFTR channel. The mutated CFTR protein is properly trafficked and localized to the plasma membrane but cannot be activated, or it cannot function as a chloride channel. In particular, Class III mutation(s) refers to p.Gly551Asp (G551D), G551S, R553G, G1349D, S1251N, G178R, S549N mutations. More particularly, Class III mutation(s) refers to G551D, R553G, G1349D, S1251N, G178R, or S549N mutations.

[0059] As used herein, "Class IV mutation(s)" refers to mutations which affect chloride conductance. The CFTR protein is correctly trafficked to the cell membrane but generates reduced chloride flow or a "gating defect" (most are missense mutations located within the membrane-spanning domain). In particular, Class IV mutation(s) refers to p.Arg117His (R117H), R347P, or p.Arg334Trp (R334W) mutations.

[0060] As used herein, "Class V mutation(s)" refers to mutations which reduce the level of normally functioning CFTR at the apical membrane or result in a "conductance defect" (for example partially aberrant splicing mutations or inefficient trafficking missense mutations). In particular, Class V mutation(s) refers to c.1210-12T[5] (5T allele), c.S3140-26A>G (3272-26A>G), c.3850-2477C>T (3849+10kbC>T) mutations.

[0061] As used herein, "Class VI mutation(s)" refers to mutations which decrease the stability of the CFTR which is present or which affect the regulation of other channels, resulting in inherent instability of the CFTR protein. In effect, although functional, the CFTR protein is unstable at the cell surface and it is rapidly removed and degraded by cell machinery. In particular, Class VI mutation(s) refers to Rescued F508del, 120del23, N287Y, 4326dellTC, or 4279insA mutations. More particularly, Class VI mutation(s) refers to Rescued F508del mutations.

Compounds

[0062] Compounds of the invention have the general formula (I) as described above.

[0063] Particular values of variable groups in compounds of formula (I) are as follows. Such values may be used where appropriate with any of the other values, definitions, claims or embodiments defined hereinbefore or hereinafter.

[0064] In certain embodiments of formula (I), R^1 is G^{1A}, C_1-C_6 haloalkyl, or C_1-C_6 alkyl.

[0065] In certain embodiments of formula (I), R^1 is G^{1A}.

[0066] In certain embodiments of formula (I), R^1 is G^{1A} wherein G^{1A} is phenyl, pyrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, azetidinyl, oxetanyl, tetrahydrofuranyl, pyrrolidinyl, dihydropyranyl,1,6-dihydropyridazinyl, tetrahydropyranyl, tetrahydrothienyl, piperidinyl, cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl.

[0067] In certain embodiments of formula (I), R^1 is G^{1A} wherein G^{1A} is phenyl, pyridinyl, tetrahydrofuranyl, tetrahydropyranyl, cyclopropyl, cyclopentyl, or cyclohexyl.

[0068] In certain embodiments of formula (I), R^1 is G^{1A} wherein G^{1A} is phenyl, pyridinyl, or cyclohexyl.

[0069] In certain embodiments of formula (I), R^1 is G^{1A} wherein G^{1A} is 4-7 membered monocyclic heterocycle. In some such embodiments, the 4-7 membered monocyclic heterocycle is tetrahydrofuranyl or tetrahydropyranyl.

[0070] In certain embodiments of formula (I), R^1 is G^{1A} wherein G^{1A} is C_3-C_6 monocyclic cycloalkyl. In some such embodiments, the C_3-C_6 monocyclic cycloalkyl is cyclohexyl. In some such embodiments, the C_3-C_6 monocyclic cycloalkyl is cyclopentyl. In some such embodiments, the C_3-C_6 monocyclic cycloalkyl is cyclopropyl.

[0071] In certain embodiments, R^1 is G^{1A} wherein G^{1A} is 5-11 membered fused bicyclic heterocycle. In some such embodiments, the 5-11 membered fused bicyclic heterocycle is 1,3-benzodioxolyl.

[0072] In certain embodiments of formula (I), R^1 is G^{1A} wherein G^{1A} is phenyl or 5-6 membered monocyclic heteroaryl. In some such embodiments, the 5-6 membered monocyclic heteroaryl is pyridinyl, pyrimidinyl, pyrazinyl, or pyridazinyl. In some such embodiments, the 5-6 membered monocyclic heteroaryl is pyridinyl or pyrimidinyl. In some such embodiments, the 5-6 membered monocyclic heteroaryl is pyridinyl.

[0073] In certain embodiments of formula (I), R^1 is G^{1A} wherein G^{1A} is phenyl.

[0074] In certain embodiments of formula (I), R^1 is G^{1A} wherein G^{1A} is 5-6 membered monocyclic heteroaryl. In some such embodiments, the 5-6 membered monocyclic heteroaryl is pyridinyl, pyrimidinyl, pyrazinyl, or pyridazinyl. In some such embodiments, the 5-6 membered monocyclic heteroaryl is pyridinyl or pyrimidinyl. In some such embodiments, the 5-6 membered monocyclic heteroaryl is pyridinyl.

[0075] In certain embodiments, G^{1A}, including the exemplary rings, are optionally substituted with 1, 2, 3, or 4 substituents independently selected from the group consisting of R^{1a} and G^{1B}.

[0076] In certain embodiments, G^{1A}, including the exemplary rings, are optionally substituted with 1, 2, 3, or 4 independently selected R^{1a}.

[0077] In certain embodiments, G^{1A}, including the exemplary rings, are optionally substituted with 1, 2, or 3 independently selected R^{1a}.

[0078] In certain embodiments, G^{1A}, including the exemplary rings, are optionally substituted with 1 or 2 independently selected R^{1a}.

[0079] In certain embodiments, G^{1A}, including the exemplary rings, are unsubstituted.

[0080] In certain embodiments, G^{1A}, including the exemplary rings, are substituted with one G^{1B}, and said G^{1A}, including the exemplary rings, are optionally further substituted with 1, 2, or 3 independently selected R^{1a}. In some such embodiments, said G^{1A}, including the exemplary rings, are optionally further substituted with 1 or 2 independently selected R^{1a}. In some such embodiments, said G^{1A}, including the exemplary rings, are optionally further substituted with one R^{1a}. In some such embodiments, said G^{1A}, including the exemplary rings, are not further substituted.

[0081] In certain embodiments of formula (I), each R^{1a} is independently C_1-C_6 alkyl, halogen, C_1-C_6 haloalkyl, oxo, -CN, -OR^m, -$S(O)_2R^m$, -$S(O)_2N(R^m)_2$, -$C(O)R^m$, -$C(O)OR^m$, -$C(O)N(R^m)_2$, -$N(R^m)_2$, –$N(R^m)$(alkoxyalkyl), –N(alkoxyalkyl)$_2$, or -(C_1-C_6 alkylenyl-CN).

[0082] In certain embodiments of formula (I), each R^{1a} is independently C_1-C_6 alkyl, halogen, C_1-C_6 haloalkyl, -CN, -OR^m, -$N(R^m)_2$, –$N(R^m)$(alkoxyalkyl), or –N(alkoxyalkyl)$_2$.

[0083] In certain embodiments of formula (I), each R^{1a} is independently C_1-C_3 alkyl, halogen, C_1-C_3 haloalkyl, -CN, -OR^m, or -$N(R^m)_2$.

[0084] In certain embodiments of formula (I), G^{1B} is a 4-7 membered monocyclic heterocycle.

[0085] In certain embodiments of formula (I), G^{1B} is azetidinyl, pyrrolidinyl, piperidinyl, tetrahydropyranyl, or morpholinyl.

[0086] In certain embodiments, G^{1B}, including the exemplary rings, are optionally substituted with 1, 2, 3, or 4 independently selected R^{1b} groups.

[0087] In certain embodiments, G^{1B}, including the exemplary rings, are optionally substituted with 1, 2, or 3 independently selected R^{1b} groups.

[0088] In certain embodiments, G^{1B}, including the exemplary rings, are optionally substituted with 1 or 2 independently selected R^{1b}.

[0089] In certain embodiments, G^{1B}, including the exemplary rings, are unsubstituted.

[0090] In certain embodiments of formula (I), each R^{1b} is independently C_1-C_3 alkyl, halogen, C_1-C_3 haloalkyl, or -OR^m.

[0091] In certain embodiments of formula (I), R^1 is C_1-C_6 alkyl. In some such embodiments, R^1 is –$C(CH_3)_3$, -$C(H)(CH_3)_2$, or –CH_2-$CH(CH_3)_2$. In some such embodiments, R^1 is -$C(H)(CH_3)_2$ or –CH_2-$CH(CH_3)_2$. In some such embodiments, R^1 is -$C(H)(CH_3)_2$.

[0092] In certain embodiments of formula (I), R^1 is C_1-C_6 alkyl substituted with one G^{1A}. In some such embodiments, G^{1A} is optionally substituted C_3-C_6 monocyclic cycloalkyl. In some such embodiments, G^{1A} is optionally substituted cyclobutyl. In some such embodiments, G^{1A} is unsubstituted cyclobutyl.

[0093] In certain embodiments of formula (I), R^2 is C_1-C_6 alkyl, C_1-C_6 haloalkyl, -OR^{2xa}, -$N(R^{2xa})(R^{2xb})$, or G^{2A}.

[0094] In certain embodiments of formula (I), R^2 is C_1-C_6 alkyl, C_1-C_6 haloalkyl, -OR^{2xa}, or G^{2A}.

[0095] In certain embodiments of formula (I), R^2 is C_1-C_6 alkyl, C_1-C_6 haloalkyl, or G^{2A}.

[0096] In certain embodiments of formula (I), R^2 is C_1-C_6 alkyl or G^{2A}.

[0097] In certain embodiments of formula (I), R^2 is $-CH_3$, $-C(H)(CH_3)_2$, $-C(CH_3)_3$, or G^{2A}.

[0098] In certain embodiments of formula (I), R^2 is $-CH_3$, $-C(H)(CH_3)_2$, or G^{2A}.

[0099] In certain embodiments of formula (I), R^2 is $-C(H)(CH_3)_2$ or G^{2A}.

[00100] In certain embodiments of formula (I), R^2 is C_1-C_6 alkyl.

[00101] In certain embodiments of formula (I), R^2 is $-CH_3$, $-C(H)(CH_3)_2$, or $-C(CH_3)_3$.

[00102] In certain embodiments of formula (I), R^2 is $-CH_3$ or $-C(H)(CH_3)_2$.

[00103] In certain embodiments of formula (I), R^2 is G^{2A}.

[00104] In certain embodiments, G^{2A} is a C_3-C_6 monocyclic cycloalkyl. In some such embodiments, G^{2A} is cyclopropyl or cyclobutyl. In some such embodiments, G^{2A} is cyclobutyl.

[00105] In certain embodiments, G^{2A} is a 4-7 membered monocyclic heterocycle. In some such embodiments, G^{2A} is azetidinyl, oxetanyl, pyrrolidinyl, or tetrahydrofuranyl. In some such embodiments, G^{2A} is azetidinyl or oxetanyl. In some such embodiments, G^{2A} is azetidinyl.

[00106] In certain embodiments, G^{2A} is azetidinyl, oxetanyl, pyrrolidinyl, tetrahydrofuranyl, cyclopropyl, or cyclobutyl.

[00107] In certain embodiments, G^{2A} is azetidinyl, pyrrolidinyl, cyclopropyl, or cyclobutyl.

[00108] In certain embodiments, G^{2A} is azetidinyl or cyclobutyl.

[00109] In certain embodiments, G2A is azetidinyl.

[00110] In certain embodiments, G^{2A} is cyclobutyl.

[00111] In certain embodiments of formula (I), G^{2A}, including the exemplary rings, are optionally substituted with 1, 2, or 3 independently selected R^{2a} groups.

[00112] In certain embodiments of formula (I), G^{2A}, including the exemplary rings, are optionally substituted with 1 or 2 independently selected R^{2a} groups.

[00113] In certain embodiments of formula (I), G^{2A}, including the exemplary rings, are unsubstituted.

[00114] In certain embodiments of formula (I), R^2 is $-OR^{2xa}$.

[00115] In certain embodiments of formula (I), R^2 is $-OR^{2xa}$ wherein R^{2xa} is C_1-C_6 alkyl or G^{2B}.

[00116] In certain embodiments, G^{2B} is a 4-7 membered monocyclic heterocycle.

[00117] In certain embodiments, G^{2B} is azetidinyl, pyrrolidinyl, piperidinyl, oxetanyl, tetrahydrofuranyl, or tetrahydropyranyl.

[00118] In certain embodiments, G^{2B} is piperidinyl, oxetanyl, or tetrahydrofuranyl.

[00119] In certain embodiments, G^{2B} is oxetanyl.

[00120] In certain embodiments, G^{2B} is a C_3-C_6 monocyclic cycloalkyl. In some such embodiments, the C_3-C_6 monocyclic cycloalkyl is cyclobutyl.

[00121] In certain embodiments of formula (I), G^{2B}, including the exemplary rings, are optionally substituted with 1, 2, or 3 independently selected R^{2a} groups.

[00122] In certain embodiments of formula (I), G^{2B}, including the exemplary rings, are optionally substituted with 1 or 2 independently selected R^{2a} groups.

[00123] In certain embodiments of formula (I), G^{2B}, including the exemplary rings, are unsubstituted.

[00124] In certain embodiments of formula (I), each R^{2a} is independently C_1-C_6 alkyl, halogen, C_1-C_6 haloalkyl, oxo, -CN, -OR^m, -$C(O)R^m$, -$C(O)OR^m$, or -(C_1-C_6 alkylenyl)-CN.

[00125] In certain embodiments of formula (I), each R^{2a} is independently C_1-C_3 alkyl, halogen, C_1-C_3 haloalkyl, -OR^m, or -$C(O)OR^m$.

[00126] In certain embodiments of formula (I), R^3 is G^{3A}, -G^{3B}-L^1-G^{3C}, -G^{3B}-L^3-G^{3C}-G^{3E}, -(C_1-C_6 alkylenyl)-G^{3D}, or –OR^{3a}.

[00127] In certain embodiments of formula (I), R^3 is G^{3A}, -G^{3B}-L^1-G^{3C}, or –OR^{3a}.

[00128] In certain embodiments of formula (I), R^3 is G^{3A} or -G^{3B}-L^1-G^{3C}.

[00129] In certain embodiments of formula (I), R^3 is G^{3A}.

[00130] In certain embodiments of formula (I), R^3 is G^{3A} wherein G^{3A} is phenyl, 5-6 membered monocyclic heteroaryl, or 4-11 membered heterocycle.

[00131] In certain embodiments of formula (I), R^3 is G^{3A} wherein G^{3A} is phenyl or 5-6 membered monocyclic heteroaryl.

[00132] In certain embodiments of formula (I), R^3 is G^{3A} wherein G^{3A} is phenyl, pyrazolyl, pyrrolyl, pyridinyl, pyrimidinyl, pyridazinyl, or pyrazinyl.

[00133] In certain embodiments of formula (I), R^3 is G^{3A} wherein G^{3A} is phenyl, pyridinyl, pyrimidinyl, pyridazinyl, or pyrazinyl.

[00134] In certain embodiments of formula (I), R^3 is G^{3A} wherein G^{3A} is phenyl, pyridinyl, or pyrimidinyl.

[00135] In certain embodiments of formula (I), R^3 is G^{3A} wherein G^{3A} is phenyl.

[00136] In certain embodiments of formula (I), R^3 is G^{3A} wherein G^{3A} is pyridinyl.

[00137] In certain embodiments of formula (I), R^3 is G^{3A} wherein G^{3A} is a 4-11 membered heterocycle.

[00138] In certain embodiments of formula (I), R^3 is G^{3A} wherein G^{3A} is azetidinyl, pyrrolidinyl, piperidinyl, dihydropyranyl, piperazinyl, morpholinyl, thiomorpholinyl, tetrahydropyridinyl, azepanyl, 1,4-oxazepanyl, 1,4-diazepanyl, 2-azaspiro[3.3]heptyl, 2-oxaspiro[3.3]heptyl, 5-azaspiro[2.4]heptyl, 2-azaspiro[3.4]octyl, 5-azaspiro[2.5]octyl, 5-azaspiro[3.4]octyl, 5-oxa-2-azaspiro[3.5]nonyl, 6-oxa-2-azaspiro[3.4]octyl, 6-oxa-2-azaspiro[3.5]nonyl, 7-oxa-2-azaspiro[3.5]nonyl, 1-oxa-7-azaspiro[3.5]nonyl, 1-oxa-7-azaspiro[4.4]nonyl, 2-oxa-7-azaspiro[3.5]nonyl, 7-azaspiro[3.5]nonyl, 2,7-diazaspiro[4.4]nonyl, 2-azaspiro[3.5]nonyl, 1,3,8-triazaspiro[4.5]decyl, 8-azaspiro[4.5]decyl, 8-oxa-2-azaspiro[4.5]decyl, 1-oxa-8-azaspiro[4.5]decyl, 1-oxa-3,8-diazaspiro[4.5]decyl, 1-oxa-4,9-diazaspiro[5.5]undecyl, 1,4-dioxa-8-azaspiro[4.5]decyl, 3-azaspiro[5.5]undecyl, 3-azabicyclo[3.1.0]hexyl, 8-azabicyclo[3.2.1]octyl, octahydropyrrolo[3,4-*c*]pyrrolyl, hexahydro-1*H*-oxazolo[3,4-*a*]pyrazinyl, octahydropyrrolo[1,2-*a*]pyrazinyl, octahydroimidazo[1,5-*a*]pyrazinyl, octahydro-1*H*-pyrrolo[3,2-*c*]pyridinyl, decahydropyrrolo[3,4-*b*]azepinyl, or isoindolinyl.

[00139] In certain embodiments of formula (I), R^3 is G^{3A} wherein G^{3A} is azetidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, 2-azaspiro[3.3]heptyl, 5-azaspiro[2.4]heptyl, 2-azaspiro[3.4]octyl, 5-azaspiro[2.5]octyl, 5-oxa-2-azaspiro[3.5]nonyl, 6-oxa-2-azaspiro[3.5]nonyl, 7-oxa-2-azaspiro[3.5]nonyl, 1-oxa-7-azaspiro[3.5]nonyl, 2-azaspiro[3.5]nonyl, 1,3,8-triazaspiro[4.5]decyl, 8-oxa-2-azaspiro[4.5]decyl, 1-oxa-8-azaspiro[4.5]decyl, 1-oxa-3,8-diazaspiro[4.5]decyl, 3-azaspiro[5.5]undecyl, 3-azabicyclo[3.1.0]hexyl, or octahydro-1*H*-pyrrolo[3,2-*c*]pyridinyl.

[00140] In certain embodiments of formula (I), R^3 is G^{3A} is a 4-7 membered monocyclic heterocycle.

[00141] In certain embodiments of formula (I), R^3 is G^{3A} wherein G^{3A} is azetidinyl, pyrrolidinyl, piperidinyl, dihydropyranyl, piperazinyl, morpholinyl, thiomorpholinyl, tetrahydropyridinyl, azepanyl, 1,4-oxazepanyl, or 1,4-diazepanyl.

[00142] In certain embodiments of formula (I), R^3 is G^{3A} wherein G^{3A} is azetidinyl, piperidinyl, or piperazinyl.

[00143] In certain embodiments of formula (I), R^3 is G^{3A} wherein G^{3A} is piperidinyl or piperazinyl.

[00144] In certain embodiments of formula (I), R^3 is G^{3A} wherein G^{3A} is piperidinyl.

[00145] In certain embodiments, each of the aforementioned G^{3A}, including the exemplary rings, are optionally substituted with 1, 2, 3, or 4 independently selected R^e groups.

[00146] In certain embodiments, each of the aforementioned G^{3A}, including the exemplary rings, are optionally substituted with 1, 2, or 3 independently selected R^e groups.

[00147] In certain embodiments, each of the aforementioned G^{3A}, including the exemplary rings, are optionally substituted with 1 or 2 independently selected R^e groups.

[00148] In certain embodiments, G^{3A}, including the exemplary rings, are unsubstituted.

[00149] In certain embodiments, each of the optional substituents of G^{3A} is independently C_1-C_6 alkyl, C_1-C_6 haloalkyl, halogen, oxo, -CN, $-N_3$, $-OR^f$, $-S(O)_2R^f$, $-C(O)R^f$, $-C(O)OR^f$, $-C(O)NR^fR^h$, $-N(R^f)_2$, $-N(R^h)C(O)R^h$, $-N(R^h)S(O)_2R^g$, or $-N(R^h)C(O)O(R^g)$; wherein the C_1-C_6 haloalkyl and the C_1-C_6 alkyl are each optionally substituted with 1 or 2 substituents independently selected from the group consisting of -CN, $-OR^f$, $-N(R^f)_2$, $-C(O)N(R^f)_2$, and $-N(R^h)C(O)O(R^g)$.

[00150] In certain embodiments, each of the optional substituents of G^{3A} is independently C_1-C_6 alkyl, C_1-C_6 haloalkyl, halogen, oxo, -CN, $-N_3$, $-OR^f$, $-S(O)_2R^f$, $-C(O)OR^f$, $-N(R^f)_2$, or $-N(R^h)C(O)R^h$; wherein the C_1-C_6 haloalkyl and the C_1-C_6 alkyl are each optionally substituted with 1 or 2 substituents independently selected from the group consisting of -CN, $-OR^f$, and $-N(R^f)_2$; and each R^f is independently hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, -(C_1-C_6 alkylenyl)-OR^m, or -(C_1-C_6 alkylenyl)-$N(R^m)_2$.

[00151] In certain embodiments, each of the optional substituents of G^{3A} is independently C_1-C_6 alkyl, C_1-C_6 haloalkyl, halogen, $-OR^f$, or $-N(R^f)_2$; wherein the C_1-C_6 haloalkyl and the C_1-C_6 alkyl are each optionally substituted with 1 or 2 substituents independently selected from the group consisting of $-OR^f$ and $-N(R^f)_2$; and each R^f is independently hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, -(C_1-C_6 alkylenyl)-OR^m, or -(C_1-C_6 alkylenyl)-$N(R^m)_2$.

[00152] In certain embodiments of formula (I), R^3 is $-G^{3B}$-L^1-G^{3C}.

[00153] In certain embodiments of formula (I), G^{3B} is phenyl, 5-6 membered monocyclic heteroaryl, or 4-7 membered monocyclic heterocycle.

[00154] In certain embodiments of formula (I), G^{3B} is phenyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, 1-oxa-8-azaspiro[4.5]decyl, 3,9-diazaspiro[5.5]undecyl, octahydro-1*H*-pyrrolo[3,2-*c*]pyridinyl, or 1,4-diazepanyl.

[00155] In certain embodiments of formula (I), G^{3B} is phenyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, piperidinyl, or piperazinyl.

[00156] In certain embodiments of formula (I), G^{3B} is phenyl, pyridinyl, pyrimidinyl, piperidinyl, or piperazinyl.

[00157] In certain embodiments of formula (I), G^{3B} is a 4-7 membered monocyclic heterocycle.

[00158] In certain embodiments of formula (I), G^{3B} is azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, or 1,4-diazepanyl.

[00159] In certain embodiments of formula (I), G^{3B} is piperidinyl or piperazinyl.

[00160] In certain embodiments of formula (I), G^{3B} is piperidinyl.

[00161] In certain embodiments of formula (I), G^{3B} is piperazinyl.

[00162] In certain embodiments of formula (I), G^{3C} is C_3-C_6 monocyclic cycloalkyl, phenyl, 5-6 membered monocyclic heteroaryl, or 4-7 membered monocyclic heterocycle.

[00163] In certain embodiments of formula (I), G^{3C} is cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, phenyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, azetidinyl, oxetanyl, pyrrolidinyl, tetrahydrofuranyl, oxazolidinyl, piperidinyl, piperazinyl, tetrahydropyranyl, thiomorpholinyl, 2-oxa-5,8-diazaspiro[3.5]nonyl, 2-oxa-5-azabicyclo[2.2.1]heptyl, hexahydropyrrolo[3,4-*c*]pyrrolyl, or morpholinyl.

[00164] In certain embodiments of formula (I), G^{3C} is 4-7 membered monocyclic heterocycle.

[00165] In certain embodiments of formula (I), G^{3C} is azetidinyl, oxetanyl, pyrrolidinyl, tetrahydrofuranyl, oxazolidinyl, piperidinyl, piperazinyl, tetrahydropyranyl, thiomorpholinyl, or morpholinyl.

[00166] In certain embodiments of formula (I), G^{3C} is azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, tetrahydropyranyl, tetrahydropyranyl, or morpholinyl.

[00167] In certain embodiments of formula (I), G^{3C} is pyrrolidinyl, piperidinyl, piperazinyl, or morpholinyl.

[00168] In certain embodiments, each of the aforementioned G^{3B} and G^{3C}, including the exemplary rings, are optionally substituted with 1, 2, 3, or 4 independently selected R^e groups.

[00169] In certain embodiments, each of the aforementioned G^{3B} and G^{3C}, including the exemplary rings, are optionally substituted with 1, 2, or 3 independently selected R^e groups.

[00170] In certain embodiments, each of the aforementioned G^{3B} and G^{3C}, including the exemplary rings, are optionally substituted with 1 or 2 independently selected R^e groups.

[00171] In certain embodiments, G^{3B} and G^{3C}, including the exemplary rings, are unsubstituted.

[00172] In certain embodiments, each of the optional substituents of G^{3B} is independently C_1-C_6 alkyl, C_1-C_6 haloalkyl, halogen, -OR^f, or –CN. In some such embodiments, R^f is hydrogen, C_1-C_3 alkyl, or C_1-C_3 haloalkyl.

[00173] In certain embodiments, each of the optional substituents of G^{3B} is independently -CH_3, -CH_2F, -CHF_2, -CF_3, or F.

[00174] In certain embodiments, each of the optional substituents of G^{3C} is independently C_1-C_6 alkyl, C_1-C_6 haloalkyl, halogen, oxo, -OR^f, -$N(R^f)_2$, -$C(O)OR^f$, or –CN; wherein the C_1-C_6 alkyl is optionally substituted with one -OR^f.

[00175] In certain embodiments, each of the optional substituents of G^{3C} is independently -CH_3, -CH_2F, -CHF_2, -CF_3, F, or –CN.

[00176] In certain embodiments, L^1 is a bond, C_1-C_3 alkylenyl, or (C_1-C_3 alkylenyl)$_r$-L^2-(C_1-C_3 alkylenyl)$_s$.

[00177] In certain embodiments, L^2 is O, $N(R^x)$, or C(O).

[00178] In certain embodiments, L^2 is O or $N(R^x)$.

[00179] In certain embodiments of formula (I), R^3 is –OR^{3a}.

[00180] In certain embodiments of formula (I), R^3 is –OR^{3a} wherein R^{3a} is G^{3D}, C_1-C_6 haloalkyl, or C_1-C_6 alkyl; wherein the C_1-C_6 haloalkyl and the C_1-C_6 alkyl are each substituted with one or two substituents independently selected from the group consisting of G^{3D}, -OR^{3xa}, and -$N(R^{3xb})_2$.

[00181] In certain embodiments of formula (I), R^3 is –OR^{3a}; and R^{3a} is C_1-C_6 haloalkyl and C_1-C_6 alkyl; wherein the C_1-C_6 haloalkyl and the C_1-C_6 alkyl are each substituted with one G^{3D}.

[00182] In certain embodiments, G^{3D} is oxetanyl, pyrrolidinyl, tetrahydrofuranyl, imidazolidinyl, tetrahydropyranyl, piperidinyl, piperazinyl, thiomorpholinyl, morpholinyl, 1,3-dioxolanyl, azepanyl, 1,4-diazepanyl, 1,3-dioxanyl, 1,4-dioxanyl, 8-azaspiro[4.5]decyl, cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl.

[00183] In certain embodiments, G^{3D} is a 4-7 membered monocyclic heterocycle.

[00184] In certain embodiments, G^{3D} is oxetanyl, pyrrolidinyl, tetrahydrofuranyl, imidazolidinyl, tetrahydropyranyl, piperidinyl, piperazinyl, thiomorpholinyl, morpholinyl, 1,3-dioxolanyl, azepanyl, 1,4-diazepanyl, 1,3-dioxanyl, or 1,4-dioxanyl.

[00185] In certain embodiments, G^{3D} is tetrahydrofuranyl, tetrahydropyranyl, piperidinyl, piperazinyl, thiomorpholinyl, morpholinyl, or 1,4-dioxanyl.

[00186] In certain embodiments, G^{3D} is tetrahydropyranyl.

[00187] In certain embodiments, each of the aforementioned G^{3D}, including the exemplary rings, are optionally substituted with 1, 2, 3, or 4 independently substituents independently selected from the group consisting of R^e and G^{3E}.

[00188] In certain embodiments, each of the aforementioned G^{3D}, including the exemplary rings, are optionally substituted with 1, 2, or 3 independently selected R^e groups.

[00189] In certain embodiments, each of the aforementioned G^{3D}, including the exemplary rings, are optionally substituted with 1 or 2 independently selected R^e groups.

[00190] In certain embodiments, each of the aforementioned G^{3D}, including the exemplary rings, are optionally substituted with one G^{3E} and optionally with 1 or 2 independently selected R^e groups. Examples of G^{3E} include cyclobutyl, cyclohexyl, and tetrahydropyranyl, each of which is optionally substituted.

[00191] In certain embodiments, G^{3D}, including the exemplary rings, are unsubstituted. In certain embodiments, each of the R^e groups of G^{3D} is independently C_1-C_6 alkyl, C_1-C_6 haloalkyl, halogen, oxo, $-OR^f$, $-C(O)R^f$, $-C(O)OR^f$, or –CN.

[00192] In certain embodiments of formula (I), R^3 is $-N(R^{3a})(R^{3b})$.

[00193] In certain embodiments of formula (I), R^3 is $-N(R^{3a})(R^{3b})$ wherein R^{3a} is C_1-C_3 haloalkyl or C_1-C_3 alkyl; wherein the C_1-C_3 haloalkyl and the C_1-C_3 alkyl are each substituted with one substituent independently selected from the group consisting of $-OR^{3xa}$ and $-N(R^{3xb})_2$. In some such embodiments, R^{3xa} and R^{3xb}, at each occurrence, are each independently hydrogen, C_1-C_3 haloalkyl, or C_1-C_3 alkyl.

[00194] In certain embodiments of formula (I), R^3 is $-G^{3B}$-L^3-G^{3C}-G^{3E}. In some such embodiments, G^{3B} is phenyl, 5-6 membered heteroaryl, or 4-11 membered heterocycle, G^{3C} is 4-11 membered heterocycle; and G^{3E} is C_3-C_8 monocyclic cycloalkyl. Examples of G^{3B} are phenyl, pyridinyl, piperidinyl, and piperazinyl. In some such embodiments, G^{3C} is piperidinyl or piperazinyl. In some such embodiments, G^{3E} is cyclopropyl. G^{3B}, G^{3C}, and G^{3E}, including the exemplary rings, are each optionally substituted as described in the summary and embodiments herein above.

[00195] In certain embodiments, R^3 is-(C_1-C_6 alkylenyl)-G^{3D}. In some such embodiments, G^{3D} is 4-7 membered monocyclic heterocycle. In some such embodiments, G^{3D} is piperidinyl, piperazinyl or morpholinyl. G^{3D}, including the exemplary rings are each optionally substituted as described in the Summary and embodiments herein above.

[00196] In certain embodiments of formula (I), R^4 is hydrogen or C_1-C_3 alkyl.

[00197] In certain embodiments of formula (I), R^4 is hydrogen.

[00198] In certain embodiments of formula (I), R^5 is C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, or C_1-C_6 haloalkyl; wherein the C_1-C_6 alkyl and the C_1-C_6 haloalkyl are each optionally substituted with one or two substituents independently selected from the group consisting of G^{5A}, -CN, $-N_3$, $-OR^{5ax}$, $-S(O)_2R^{5ax}$, $-S(O)_2N(R^{5ax})(R^{5bx})$, $-N(R^{5ax})(R^{5bx})$, $-N(R^{5bx})S(O)_2R^{5cx}$, $-N(R^{5bx})C(O)R^{5cx}$, $-N(R^{5bx})C(O)N(R^{5ax})(R^{5bx})$, $-N(R^{5bx})C(O)OR^{5cx}$, $-C(O)R^{5ax}$, $-C(O)OR^{5ax}$, $-C(O)N(R^{5bx})S(O)_2R^{5cx}$, and $-C(O)N(R^{5ax})(R^{5bx})$.

[00199] In certain embodiments of formula (I), R^5 is C_1-C_6 alkyl or C_1-C_6 haloalkyl.

[00200] In certain embodiments of formula (I), R^5 is $-CH_3$, $-CH_2CH_3$, $-CH_2C(H)C(CH_3)_2$, $-C(CH_3)_3$, $-CF_3$, $-CH_2Cl$, $-CH_2CF_3$, or $-CH_2CH_2CF_3$.

[00201] In certain embodiments of formula (I), R^5 is $-CH_3$.

[00202] In certain embodiments of formula (I), R^5 is C_1-C_6 alkyl which is substituted with one substituent selected from the group consisting of G^{5A}, -CN, $-N_3$, $-OR^{5ax}$, $-S(O)_2R^{5ax}$, $-S(O)_2N(R^{5ax})(R^{5bx})$, $-N(R^{5ax})(R^{5bx})$, $-N(R^{5bx})S(O)_2R^{5cx}$, $-N(R^{5bx})C(O)R^{5cx}$, $-N(R^{5bx})C(O)N(R^{5ax})(R^{5bx})$, $-N(R^{5bx})C(O)OR^{5cx}$, $-C(O)R^{5ax}$, $-C(O)OR^{5ax}$, $-C(O)N(R^{5bx})S(O)_2R^{5cx}$, and $-C(O)N(R^{5ax})(R^{5bx})$.

[00203] In certain embodiments of formula (I), R^5 is C_1-C_6 alkyl which is substituted with one substituent selected from the group consisting of G^{5A}, -CN, $-N_3$, $-OR^{5ax}$, $-N(R^{5ax})(R^{5bx})$, $-N(R^{5bx})C(O)R^{5cx}$, $-N(R^{5bx})C(O)OR^{5cx}$, $-C(O)OR^{5ax}$, and $-C(O)N(R^{5ax})(R^{5bx})$.

[00204] In certain embodiments of formula (I), R^5 is C_1-C_6 alkyl substituted with one G^{5A}. In some such embodiments, G^{5A} is 5-6 membered monocyclic heteroaryl or a 4-11 membered heterocycle.

[00205] In certain embodiments of formula (I), R^5 is $-N(R^{5ax})(R^{5bx})$. In some such embodiments, R^{5ax} is hydrogen, C_1-C_6 alkyl, or C_1-C_6 haloalkyl; and R^{5bx} is C_1-C_6 alkyl, C_1-C_6 haloalkyl or G^{5A}. In some such embodiments, R^{5ax} and R^{5bx} are each C_1-C_6 alkyl.

[00206] In certain embodiments of formula (I), R^5 is G^{5A}.

[00207] In certain embodiments of formula (I), R^5 is G^{5A} wherein G^{5A} is C_3-C_6 monocyclic cycloalkyl, phenyl, 5-6 membered monocyclic heteroaryl, or 4-11 membered heterocycle.

[00208] In certain embodiments, each of the aforementioned G^{5A} is optionally substituted with 1, 2, 3, or 4 independently selected R^{5a} groups.

[00209] In certain embodiments, G^{5A} is optionally substituted with 1, 2, or 3, independently selected R^{5a} groups.

[00210] In certain embodiments, G^{5A} is optionally substituted with 1, or 2 independently selected R^{5a} groups.

[00211] In certain embodiments, G^{5A} is unsubstituted.

[00212] In certain embodiments of formula (I), R^6 is hydrogen.

[00213] In certain embodiments of formula (I), R^6 is C_1-C_6 alkyl or C_1-C_6 haloalkyl.

[00214] In certain embodiments of formula (I), R^6 is C_1-C_6 alkyl. In some such embodiments, R^6 is $-CH_3$.

[00215] In certain embodiments of formula (I), R^5 and R^6 together form a C_1-C_6 alkylenyl or $-N(R^z)$-(C_1-C_6 alkylenyl)- wherein the $N(R^z)$ is attached to the $S(O)_2$ moiety of formula (I).

[00216] In certain embodiments of formula (I), R^5 and R^6 together form a C_1-C_6 alkylenyl.

[00217] In certain embodiments of formula (I), R^5 and R^6 together form a $-N(R^z)$-(C_1-C_6 alkylenyl)- wherein the $N(R^z)$ is attached to the $S(O)_2$ moiety of formula (I).

[00218] Various embodiments of substituents R^1, R^2, R^3, R^4, R^5, R^6, G^{1A}, R^{1a}, G^{1B}, R^{1b}, G^{2A}, G^{2B}, R^{2a}, R^{2xa}, G^{3A}, G^{3B}, G^{3C}, R^e, R^f, L^1, L^2, R^{3a}, G^{3D}, G^{5A}, R^{5ax}, and R^{5bx} have been discussed above. These substituents embodiments can be combined to form various embodiments of the invention. All embodiments of present compounds, formed by combining the substituent embodiments discussed above are within the scope of Applicant's invention, and some illustrative embodiments of present compounds are provided below.

[00219] In one embodiment, the invention is directed to compounds wherein R^1 is G^{1A}, C_1-C_6 haloalkyl, or C_1-C_6 alkyl; and R^2 is C_1-C_6 alkyl, C_1-C_6 haloalkyl, or G^{2A}. In some such embodiments, R^6 is hydrogen. In some such embodiments, R^6 is C_1-C_6 alkyl or C_1-C_6 haloalkyl. In some such embodiments, R^6 is C_1-C_6 alkyl. In some such embodiments, R^6 is $-CH_3$. In some such embodiments, R^5 and R^6 together form a C_1-C_6 alkylenyl or $-N(R^z)-(C_1$-C_6 alkylenyl)- wherein the $N(R^z)$ is attached to the $S(O)_2$ moiety of formula (I).

[00220] In one embodiment, the invention is directed to compounds wherein R^1 is G^{1A}; and R^2 is C_1-C_6 alkyl or G^{2A}. In some such embodiments, R^6 is hydrogen. In some such embodiments, R^6 is C_1-C_6 alkyl or C_1-C_6 haloalkyl. In some such embodiments, R^6 is C_1-C_6 alkyl. In some such embodiments, R^6 is $-CH_3$. In some such embodiments, R^5 and R^6 together form a C_1-C_6 alkylenyl or $-N(R^z)-(C_1$-C_6 alkylenyl)- wherein the $N(R^z)$ is attached to the $S(O)_2$ moiety of formula (I).

[00221] In one embodiment, the invention is directed to compounds wherein R^1 is G^{1A} wherein G^{1A} is phenyl or 5-6 membered monocyclic heteroaryl; and R^2 is C_1-C_6 alkyl or G^{2A} wherein G^{2A} is C_3-C_6 monocyclic cycloalkyl. In some such embodiments, R^6 is hydrogen. In some such embodiments, R^6 is C_1-C_6 alkyl or C_1-C_6 haloalkyl. In some such embodiments, R^6 is C_1-C_6 alkyl. In some such embodiments, R^6 is $-CH_3$. In some such embodiments, R^5 and R^6 together form a C_1-C_6 alkylenyl or $-N(R^z)-(C_1$-C_6 alkylenyl)- wherein the $N(R^z)$ is attached to the $S(O)_2$ moiety of formula (I).

[00222] In one embodiment, the invention is directed to compounds wherein R^1 is G^{1A} wherein G^{1A} is phenyl or pyridinyl; and R^2 is C_1-C_6 alkyl. In some such embodiments, R^6 is hydrogen. In some such embodiments, R^6 is C_1-C_6 alkyl or C_1-C_6 haloalkyl. In some such embodiments, R^6 is C_1-C_6 alkyl. In some such embodiments, R^6 is $-CH_3$. In some such embodiments, R^5 and R^6 together form a C_1-C_6 alkylenyl or $-N(R^z)-(C_1$-C_6 alkylenyl)- wherein the $N(R^z)$ is attached to the $S(O)_2$ moiety of formula (I).

[00223] In one embodiment, the invention is directed to compounds wherein R^1 is G^{1A} wherein G^{1A} is phenyl or pyridinyl; and R^2 is G^{2A} wherein G^{2A} is C_3-C_6 monocyclic cycloalkyl. In some such embodiments, R^6 is hydrogen. In some such embodiments, R^6 is C_1-C_6 alkyl or C_1-C_6 haloalkyl. In some such embodiments, R^6 is C_1-C_6 alkyl. In some such embodiments, R^6 is $-CH_3$. In some such embodiments, R^5 and R^6 together form a C_1-C_6 alkylenyl or $-N(R^z)-(C_1$-C_6 alkylenyl)- wherein the $N(R^z)$ is attached to the $S(O)_2$ moiety of formula (I).

[00224] In one embodiment, the invention is directed to compounds wherein R^1 is G^{1A} wherein G^{1A} is phenyl or pyridinyl; and R^2 is G^{2A} wherein G^{2A} is unsubstituted cyclobutyl. In some such embodiments, R^6 is hydrogen. In some such embodiments, R^6 is C_1-C_6 alkyl or C_1-C_6 haloalkyl. In some such embodiments, R^6 is C_1-C_6 alkyl. In some such embodiments, R^6 is $-CH_3$. In some such embodiments, R^5 and R^6 together form a C_1-C_6 alkylenyl or $-N(R^z)$-(C_1-C_6 alkylenyl)- wherein the $N(R^z)$ is attached to the $S(O)_2$ moiety of formula (I).

[00225] In one embodiment, the invention is directed to compounds wherein R^1 is G^{1A}; R^2 is C_1-C_6 alkyl or G^{2A}; and R^3 is G^{3A}, $-G^{3B}$-L^1-G^{3C}, or $-OR^{3a}$. In some such embodiments, R^6 is hydrogen. In some such embodiments, R^6 is C_1-C_6 alkyl or C_1-C_6 haloalkyl. In some such embodiments, R^6 is C_1-C_6 alkyl. In some such embodiments, R^6 is $-CH_3$. In some such embodiments, R^5 and R^6 together form a C_1-C_6 alkylenyl or $-N(R^z)$-(C_1-C_6 alkylenyl)- wherein the $N(R^z)$ is attached to the $S(O)_2$ moiety of formula (I).

[00226] In one embodiment, the invention is directed to compounds wherein R^1 is G^{1A}; R^2 is C_1-C_6 alkyl or G^{2A}; and R^5 is C_1-C_6 alkyl or C_1-C_6 haloalkyl. In some such embodiments, R^6 is hydrogen. In some such embodiments, R^6 is C_1-C_6 alkyl or C_1-C_6 haloalkyl. In some such embodiments, R^6 is C_1-C_6 alkyl. In some such embodiments, R^6 is $-CH_3$.

[00227] In one embodiment, the invention is directed to compounds wherein R^1 is G^{1A}; R^2 is C_1-C_6 alkyl or G^{2A}; and R^5 is C_1-C_6 alkyl which is substituted with one substituent selected from the group consisting of G^{5A}, -CN, $-N_3$, $-OR^{5ax}$, $-N(R^{5ax})(R^{5bx})$, $-N(R^{5bx})C(O)R^{5cx}$, $-N(R^{5bx})C(O)OR^{5cx}$, $-C(O)OR^{5ax}$, and $-C(O)N(R^{5ax})(R^{5bx})$. In some such embodiments, R^6 is hydrogen. In some such embodiments, R^6 is C_1-C_6 alkyl or C_1-C_6 haloalkyl. In some such embodiments, R^6 is C_1-C_6 alkyl. In some such embodiments, R^6 is $-CH_3$.

[00228] In one embodiment, the invention is directed to compounds wherein R^1 is G^{1A}; R^2 is C_1-C_6 alkyl or G^{2A}; and R^5 is $-N(R^{5ax})(R^{5bx})$. In some such embodiments, R^6 is hydrogen. In some such embodiments, R^6 is C_1-C_6 alkyl or C_1-C_6 haloalkyl. In some such embodiments, R^6 is C_1-C_6 alkyl. In some such embodiments, R^6 is $-CH_3$.

[00229] In one embodiment, the invention is directed to compounds wherein R^1 is G^{1A}; R^2 is C_1-C_6 alkyl or G^{2A}; and R^5 is G^{5A}. In some such embodiments, R^6 is hydrogen. In some such embodiments, R^6 is C_1-C_6 alkyl or C_1-C_6 haloalkyl. In some such embodiments, R^6 is C_1-C_6 alkyl. In some such embodiments, R^6 is $-CH_3$.

[00230] In one embodiment, the invention is directed to compounds wherein R^1 is G^{1A}; wherein G^{1A} is phenyl or 5-6 membered monocyclic heteroaryl; R^2 is C_1-C_6 alkyl or G^{2A}; wherein G^{2A} is a C_3-C_6 monocyclic cycloalkyl; R^3 is G^{3A}, $-G^{3B}$-L^1-G^{3C}, or $-OR^{3a}$; and R^5 is C_1-C_6 alkyl which is substituted with one substituent selected from the group consisting of G^{5A}, -CN, $-N_3$, $-OR^{5ax}$, $-N(R^{5ax})(R^{5bx})$, $-N(R^{5bx})C(O)R^{5cx}$, $-N(R^{5bx})C(O)OR^{5cx}$, $-C(O)OR^{5ax}$, and $-C(O)N(R^{5ax})(R^{5bx})$. In some such embodiments, R^6 is hydrogen. In some such embodiments, R^6 is C_1-C_6 alkyl or C_1-C_6 haloalkyl. In some such embodiments, R^6 is C_1-C_6 alkyl. In some such embodiments, R^6 is $-CH_3$.

[00231] In one embodiment, the invention is directed to compounds wherein R^1 is G^{1A}; wherein G^{1A} is phenyl or 5-6 membered monocyclic heteroaryl; R^2 is C_1-C_6 alkyl or G^{2A}; wherein G^{2A} is a C_3-C_6 monocyclic cycloalkyl; R^3 is G^{3A}, $-G^{3B}$-L^1-G^{3C}, or $-OR^{3a}$; and R^5 is C_1-C_6 alkyl or C_1-C_6 haloalkyl. In some such embodiments, R^6 is hydrogen. In some such embodiments, R^6 is C_1-C_6 alkyl or C_1-C_6 haloalkyl. In some such embodiments, R^6 is C_1-C_6 alkyl. In some such embodiments, R^6 is $-CH_3$.

[00232] In one embodiment, the invention is directed to compounds wherein R^1 is G^{1A}; wherein G^{1A} is phenyl or 5-6 membered monocyclic heteroaryl; R^2 is C_1-C_6 alkyl or G^{2A}; wherein G^{2A} is a C_3-C_6 monocyclic cycloalkyl; R^3 is G^{3A}, $-G^{3B}$-L^1-G^{3C}, or $-OR^{3a}$; and R^5 is $-N(R^{5ax})(R^{5bx})$ or $-OR^{5dx}$. In some such embodiments, R^6 is hydrogen. In some such embodiments, R^6 is C_1-C_6 alkyl or C_1-C_6 haloalkyl. In some such embodiments, R^6 is C_1-C_6 alkyl. In some such embodiments, R^6 is $-CH_3$.

[00233] In one embodiment, the invention is directed to compounds wherein R^1 is G^{1A}; wherein G^{1A} is phenyl or 5-6 membered monocyclic heteroaryl; R^2 is C_1-C_6 alkyl or G^{2A}; wherein G^{2A} is a C_3-C_6 monocyclic cycloalkyl; R^3 is G^{3A}, $-G^{3B}$-L^1-G^{3C}, or $-OR^{3a}$; and R^5 is G^{5A}. In some such embodiments, R^6 is hydrogen. In some such embodiments, R^6 is C_1-C_6 alkyl or C_1-C_6 haloalkyl. In some such embodiments, R^6 is C_1-C_6 alkyl. In some such embodiments, R^6 is $-CH_3$.

[00234] In one embodiment, the invention is directed to compounds wherein R^1 is G^{1A}; wherein G^{1A} is phenyl optionally substituted with 1, 2, 3, or 4 independently selected R^{1a}; R^2 is C_1-C_6 alkyl or G^{2A}; wherein G^{2A} is unsubstituted cyclobutyl; R^3 is G^{3A} wherein G^{3A} is a 4-11 membered heterocycle; and R^5 is C_1-C_6 alkyl. In some such embodiments, R^6 is hydrogen. In

some such embodiments, R^6 is C_1-C_6 alkyl or C_1-C_6 haloalkyl. In some such embodiments, R^6 is C_1-C_6 alkyl. In some such embodiments, R^6 is -CH_3.

[00235] In one embodiment, the invention is directed to compounds wherein R^1 is G^{1A}; wherein G^{1A} is phenyl substituted with one G^{1B}, and said phenyl is optionally further substituted with 1, 2, or 3 independently selected R^{1a}; R^2 is C_1-C_6 alkyl or G^{2A}; wherein G^{2A} is unsubstituted cyclobutyl; R^3 is G^{3A} wherein G^{3A} is a 4-11 membered heterocycle; and R^5 is C_1-C_6 alkyl. In some such embodiments, R^6 is hydrogen. In some such embodiments, R^6 is C_1-C_6 alkyl or C_1-C_6 haloalkyl. In some such embodiments, R^6 is C_1-C_6 alkyl. In some such embodiments, R^6 is -CH_3.

[00236] In one embodiment, the invention is directed to compounds wherein R^1 is G^{1A}; wherein G^{1A} is phenyl optionally substituted with 1, 2, 3, or 4 independently selected R^{1a}; R^2 is C_1-C_6 alkyl or G^{2A}; wherein G^{2A} is unsubstituted cyclobutyl; R^3 is -G^{3B}-L^1-G^{3C}; and R^5 is C_1-C_6 alkyl. In some such embodiments, R^6 is hydrogen. In some such embodiments, R^6 is C_1-C_6 alkyl or C_1-C_6 haloalkyl. In some such embodiments, R^6 is C_1-C_6 alkyl. In some such embodiments, R^6 is -CH_3.

[00237] In one embodiment, the invention is directed to compounds wherein R^1 is G^{1A}; wherein G^{1A} is phenyl optionally substituted with 1, 2, 3, or 4 independently selected R^{1a}; R^2 is C_1-C_6 alkyl or G^{2A}; wherein G^{2A} is unsubstituted cyclobutyl; R^3 is -G^{3B}-L^1-G^{3C}; G^{3B} and G^{3C} are 4-7 membered monocyclic heterocycle; and R^5 is C_1-C_6 alkyl. In some such embodiments, R^6 is hydrogen. In some such embodiments, R^6 is C_1-C_6 alkyl or C_1-C_6 haloalkyl. In some such embodiments, R^6 is C_1-C_6 alkyl. In some such embodiments, R^6 is -CH_3.

[00238] In one embodiment, the invention is directed to compounds wherein R^1 is G^{1A}; wherein G^{1A} is phenyl substituted with one G^{1B}, and said phenyl is optionally further substituted with 1, 2, or 3 independently selected R^{1a}; R^2 is C_1-C_6 alkyl or G^{2A}; wherein G^{2A} is unsubstituted cyclobutyl; R^3 is -G^{3B}-L^1-G^{3C}; G^{3B} and G^{3C} are 4-7 membered monocyclic heterocycle; and R^5 is C_1-C_6 alkyl. In some such embodiments, R^6 is hydrogen. In some such embodiments, R^6 is C_1-C_6 alkyl or C_1-C_6 haloalkyl. In some such embodiments, R^6 is C_1-C_6 alkyl. In some such embodiments, R^6 is -CH_3.

[00239] In one embodiment, the invention is directed to compounds wherein R^1 is G^{1A}; wherein G^{1A} is phenyl optionally substituted with 1, 2, 3, or 4 independently selected R^{1a}; R^2 is C_1-C_6 alkyl or G^{2A}; wherein G^{2A} is unsubstituted cyclobutyl; R^3 is –OR^{3a}; R^{3a} is C_1-C_6 alkyl or

C_1-C_6 haloalkyl wherein the C_1-C_6 alkyl and the C_1-C_6 haloalkyl are each substituted with one G^{3D}; G^{3D} is a 4-7 membered monocyclic heterocycle; and R^5 is C_1-C_6 alkyl. In some such embodiments, R^6 is hydrogen. In some such embodiments, R^6 is C_1-C_6 alkyl or C_1-C_6 haloalkyl. In some such embodiments, R^6 is C_1-C_6 alkyl. In some such embodiments, R^6 is $-CH_3$.

[00240] In one embodiment, the invention is directed to compounds wherein R^1 is G^{1A}; wherein G^{1A} is phenyl substituted with one G^{1B}, and said phenyl is optionally further substituted with 1, 2, or 3 independently selected R^{1a}; R^2 is C_1-C_6 alkyl or G^{2A}; wherein G^{2A} is unsubstituted cyclobutyl; R^3 is $-OR^{3a}$; R^{3a} is C_1-C_6 alkyl or C_1-C_6 haloalkyl wherein the C_1-C_6 alkyl and the C_1-C_6 haloalkyl are each substituted with one G^{3D}; G^{3D} is a 4-7 membered monocyclic heterocycle; and R^5 is C_1-C_6 alkyl. In some such embodiments, R^6 is hydrogen. In some such embodiments, R^6 is C_1-C_6 alkyl or C_1-C_6 haloalkyl. In some such embodiments, R^6 is C_1-C_6 alkyl. In some such embodiments, R^6 is $-CH_3$.

[00241] In one embodiment, the invention is directed to compounds wherein R^3 is $-G^{3B}$-L^3-G^{3C}-G^{3E}; G^{3B} is phenyl, 5-6 membered heteroaryl, or 4-11 membered heterocycle; each of which is optionally substituted; G^{3C} is optionally substituted 4-11 membered heterocycle; and G^{3E} is optionally substituted C_3-C_8 monocyclic cycloalkyl. In some such embodiments, R^6 is hydrogen. In some such embodiments, R^6 is C_1-C_6 alkyl or C_1-C_6 haloalkyl. In some such embodiments, R^6 is C_1-C_6 alkyl. In some such embodiments, R^6 is $-CH_3$. In some such embodiments, R^5 and R^6 together form a C_1-C_6 alkylenyl or $-N(R^z)$-(C_1-C_6 alkylenyl)- wherein the $N(R^z)$ is attached to the $S(O)_2$ moiety of formula (I).

[00242] In one embodiment, the invention is directed to compounds wherein R^1 is G^{1A}; wherein G^{1A} is phenyl, 5-6 membered monocyclic heteroaryl, or C_3-C_6 monocyclic cycloalkyl; R^2 is C_1-C_6 alkyl, $-OR^{2xa}$, or G^{2A}; wherein G^{2A} is an optionally substituted C_3-C_6 monocyclic cycloalkyl; and R^3 is G^{3A}, $-G^{3B}$-L^1-G^{3C}, $-G^{3B}$-L^3-G^{3C}- G^{3E}, -(C_1-C_6 alkylenyl)-G^{3D}, or $-OR^{3a}$. In some such embodiments, R^6 is hydrogen. In some such embodiments, R^6 is C_1-C_6 alkyl or C_1-C_6 haloalkyl. In some such embodiments, R^6 is C_1-C_6 alkyl. In some such embodiments, R^6 is $-CH_3$. In some such embodiments, R^5 and R^6 together form a C_1-C_6 alkylenyl or $-N(R^z)$-(C_1-C_6 alkylenyl)- wherein the $N(R^z)$ is attached to the $S(O)_2$ moiety of formula (I).

[00243] In one embodiment, the invention is directed to compounds wherein R^1 is G^{1A}; wherein G^{1A} is phenyl, 5-6 membered monocyclic heteroaryl, or C_3-C_6 monocyclic cycloalkyl; R^2 is C_1-C_6 alkyl, $-OR^{2xa}$, or G^{2A}; wherein G^{2A} is an optionally substituted C_3-C_6 monocyclic

cycloalkyl; R^3 is G^{3A}, $-G^{3B}-L^1-G^{3C}$, $-G^{3B}-L^3-G^{3C}-G^{3E}$, $-(C_1-C_6$ alkylenyl$)-G^{3D}$, or $-OR^{3a}$; and R^5 is C_1-C_6 alkyl or C_1-C_6 haloalkyl. In some such embodiments, R^6 is hydrogen. In some such embodiments, R^6 is C_1-C_6 alkyl or C_1-C_6 haloalkyl. In some such embodiments, R^6 is C_1-C_6 alkyl. In some such embodiments, R^6 is $-CH_3$.

[00244] In one embodiment, the invention is directed to compounds wherein

R^1 is G^{1A}, C_1-C_6 haloalkyl, or C_1-C_6 alkyl; wherein the C_1-C_6 haloalkyl and the C_1-C_6 alkyl are each optionally substituted with one G^{1A};

G^{1A}, at each occurrence, is independently phenyl, 5-6 membered monocyclic heteroaryl, 4-7 membered monocyclic heterocycle, or C_3-C_6 monocyclic cycloalkyl; wherein each G^{1A} is optionally substituted with 1, 2, 3, or 4 substituents independently selected from the group consisting of R^{1a} and G^{1B};

G^{1B}, at each occurrence, is independently 4-7 membered monocyclic heterocycle which is optionally substituted with 1, 2, 3, or 4 independently selected R^{1b} groups;

R^2 is hydrogen, C_2-C_4 alkenyl, C_1-C_6 alkyl, C_1-C_6 haloalkyl, $-OR^{2xa}$, $-N(R^{2xa})(R^{2xb})$, or G^{2A};

R^{2xa}, at each occurrence, is independently C_1-C_6 alkyl, C_1-C_6 haloalkyl, or G^{2B};

R^{2xb} is hydrogen, C_1-C_3 alkyl, or C_1-C_3 haloalkyl;

G^{2A} and G^{2B} are each independently a 4-7 membered monocyclic heterocycle or a C_3-C_6 monocyclic cycloalkyl; wherein G^{2A} and G^{2B} are each optionally substituted with 1, 2, or 3 independently selected R^{2a} groups;

R^3 is G^{3A}, $-G^{3B}-L^1-G^{3C}$, $-OR^{3a}$, or $-N(R^{3a})(R^{3b})$;

R^{3a}, at each occurrence, is independently G^{3D}, C_1-C_6 haloalkyl, or C_1-C_6 alkyl; wherein the C_1-C_6 haloalkyl and the C_1-C_6 alkyl are each optionally substituted with one or two substituents independently selected from the group consisting of G^{3D}, $-OR^{3xa}$, and $-N(R^{3xb})_2$;

R^{3xa} and R^{3xb}, at each occurrence, are each independently hydrogen, C_1-C_6 haloalkyl, C_1-C_6 alkyl, or G^{3D};

R^{3b} is hydrogen, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

L^1 is a bond, C_1-C_6 alkylenyl, $(C_1-C_6$ alkylenyl$)_r-L^2-(C_1-C_6$ alkylenyl$)_s$, or O-$(C_1-C_6$ alkylenyl$)$-C(O), wherein the left end of the L^1 moiety is attached to G^{3B};

L^2 is O, $N(R^x)$, C(O), $N(R^x)C(O)$, or $C(O)N(R^x)$; wherein each R^x is independently hydrogen, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

r is 0 or 1;

s is 0 or 1;

G^{3A}, G^{3B}, and G^{3C} and each independently C_3-C_{11} cycloalkyl, phenyl, 5-6 membered monocyclic heteroaryl, or 4-11 membered heterocycle; wherein G^{3A}, G^{3B}, and G^{3C} are each optionally substituted with 1, 2, 3, or 4 independently selected R^e groups;

G^{3D}, at each occurrence, is independently C_3-C_8 monocyclic cycloalkyl or 4-7 membered monocyclic heterocycle; wherein each G^{3D} is optionally substituted with 1, 2, 3, or 4 independently selected R^e groups;

R^4 is hydrogen, C_1-C_3 alkyl, or C_1-C_3 haloalkyl;

R^5 is C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, $-N(R^{5ax})(R^{5bx})$, or G^{5A}; wherein the C_1-C_6 alkyl and the C_1-C_6 haloalkyl are each optionally substituted with one or two substituents independently selected from the group consisting of G^{5A}, -CN, $-N_3$, $-OR^{5ax}$, $-S(O)_2R^{5ax}$, $-S(O)_2N(R^{5ax})(R^{5bx})$, $-N(R^{5ax})(R^{5bx})$, $-N(R^{5bx})S(O)_2R^{5cx}$, $-N(R^{5bx})C(O)R^{5cx}$, $-N(R^{5bx})C(O)N(R^{5ax})(R^{5bx})$, $-N(R^{5bx})C(O)OR^{5cx}$, $-C(O)R^{5ax}$, $-C(O)OR^{5ax}$, $-C(O)N(R^{5bx})S(O)_2R^{5cx}$, and $-C(O)N(R^{5ax})(R^{5bx})$;

R^{5ax} and R^{5bx}, at each occurrence, are each independently hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, G^{5A}, or -(C_1-C_6 alkylenyl)-G^{5A};

R^{5cx}, at each occurrence, is independently C_1-C_6 alkyl, C_1-C_6 haloalkyl, G^{5A}, or -(C_1-C_6 alkylenyl)-G^{5A};

G^{5A}, at each occurrence, is independently C_3-C_{11} cycloalkyl, phenyl, 5-6 membered monocyclic heteroaryl, or 4-11 membered heterocycle; wherein each G^{5A} is optionally substituted with 1, 2, 3, or 4 independently selected R^{5a} groups;

R^{5a}, at each occurrence, is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, C_1-C_6 haloalkyl, oxo, G^{5B}, -CN, NO_2, $-OR^b$, $-OC(O)R^c$, $-OC(O)N(R^d)_2$, $-SR^b$, $-S(O)_2R^b$, $-S(O)_2N(R^d)_2$, $-C(O)R^b$, $-C(O)OR^b$, $-C(O)N(R^d)_2$, $-C(O)N(R^d)S(O)_2R^c$, $-N(R^d)_2$, $-N(R^d)C(O)R^c$, $-N(R^d)S(O)_2R^c$, $-N(R^d)C(O)O(R^b)$, $-N(R^d)C(O)N(R^d)_2$, $-N(R^d)S(O)_2N(R^d)_2$, -(C_1-C_6 alkylenyl)-CN, -(C_1-C_6 alkylenyl)-G^{5B}, -(C_1-C_6 alkylenyl)-OR^b, -(C_1-C_6 alkylenyl)-$OC(O)R^c$, -(C_1-C_6

alkylenyl)-$OC(O)N(R^d)_2$, -(C_1-C_6 alkylenyl)-SR^b, -(C_1-C_6 alkylenyl)-$S(O)_2R^b$, -(C_1-C_6 alkylenyl)-$S(O)_2N(R^d)_2$, -(C_1-C_6 alkylenyl)-$C(O)R^b$, -(C_1-C_6 alkylenyl)-$C(O)OR^b$, -(C_1-C_6 alkylenyl)-$C(O)N(R^d)_2$, -(C_1-C_6 alkylenyl)-$C(O)N(R^d)S(O)_2R^c$, -(C_1-C_6 alkylenyl)-$N(R^d)_2$, -(C_1-C_6 alkylenyl)-$N(R^d)C(O)R^c$, -(C_1-C_6 alkylenyl)-$N(R^d)S(O)_2R^c$, -(C_1-C_6 alkylenyl)-$N(R^d)C(O)O(R^c)$, -(C_1-C_6 alkylenyl)-$N(R^d)C(O)N(R^d)_2$, or -(C_1-C_6 alkylenyl)-$N(R^d)S(O)_2N(R^d)_2$;

R^b and R^d, at each occurrence, are each independently hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, alkoxyalkyl, G^{5B}, or -(C_1-C_6 alkylenyl)-G^{5B};

R^c, at each occurrence, is independently C_1-C_6 alkyl, C_1-C_6 haloalkyl, alkoxyalkyl, G^{5B}, or -(C_1-C_6 alkylenyl)-G^{5B};

G^{5B}, at each occurrence, is independently C_3-C_6 monocyclic cycloalkyl, phenyl, 5-6 membered monocyclic heteroaryl, or 4-7 membered monocyclic heterocycle; wherein each G^{5B} is optionally substituted with 1, 2, 3, or 4 independently selected R^{5b} groups;

R^e, at each occurrence, is independently C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 alkyl, C_1-C_6 haloalkyl, halogen, oxo, -CN, $-N_3$, NO_2, $-OR^f$, $-OC(O)R^g$, $-OC(O)NR^fR^h$, $-SR^f$, $-S(O)_2R^f$, $-S(O)_2NR^fR^h$, $-C(O)R^f$, $-C(O)OR^f$, $-C(O)NR^fR^h$, $-C(O)N(R^h)S(O)_2R^f$, $-N(R^f)_2$, $-N(R^h)C(O)R^h$, $-N(R^h)S(O)_2R^g$, $-N(R^h)C(O)O(R^g)$, $-N(R^h)C(O)NR^fR^h$, or $-N(R^h)S(O)_2NR^fR^h$; wherein the C_1-C_6 haloalkyl and the C_1-C_6 alkyl are each optionally substituted with 1 or 2 substituents independently selected from the group consisting of -CN, NO_2, $-OR^f$, $-OC(O)R^g$, $-OC(O)NR^fR^h$, $-SR^f$, $-S(O)_2R^f$, $-S(O)_2NR^fR^h$, $-C(O)R^f$, $-C(O)OR^f$, $-C(O)NR^fR^h$, $-C(O)N(R^h)S(O)_2R^f$, $-N(R^f)_2$, $-N(R^h)C(O)R^g$, $-N(R^h)S(O)_2R^g$, $-N(R^h)C(O)O(R^g)$, $-N(R^h)C(O)NR^fR^h$, and $-N(R^h)S(O)_2NR^fR^h$;

R^f, at each occurrence, is independently hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, -(C_1-C_6 alkylenyl)-CN, -(C_1-C_6 alkylenyl)-OR^m, -(C_1-C_6 alkylenyl)-$OC(O)R^n$, -(C_1-C_6 alkylenyl)-$OC(O)N(R^m)_2$, -(C_1-C_6 alkylenyl)-SR^m, -(C_1-C_6 alkylenyl)-$S(O)_2R^m$, -(C_1-C_6 alkylenyl)-$S(O)_2N(R^m)_2$, -(C_1-C_6 alkylenyl)-$C(O)R^m$, -(C_1-C_6 alkylenyl)-$C(O)OR^m$, -(C_1-C_6 alkylenyl)-$C(O)N(R^m)_2$, -(C_1-C_6 alkylenyl)-$C(O)N(R^m)S(O)_2R^n$, -(C_1-C_6 alkylenyl)-$N(R^m)_2$, -(C_1-C_6 alkylenyl)-$N(R^m)C(O)R^n$, -(C_1-C_6 alkylenyl)-$N(R^m)S(O)_2R^n$, -(C_1-C_6 alkylenyl)-

$N(R^m)C(O)O(R^n)$, -(C_1-C_6 alkylenyl)-$N(R^m)C(O)N(R^m)_2$, or -(C_1-C_6 alkylenyl)-$N(R^m)S(O)_2N(R^m)_2$;

R^g, at each occurrence, is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, -(C_1-C_6 alkylenyl)-CN, -(C_1-C_6 alkylenyl)-OR^m, -(C_1-C_6 alkylenyl)-$OC(O)R^n$, -(C_1-C_6 alkylenyl)-$OC(O)N(R^m)_2$, -(C_1-C_6 alkylenyl)-SR^m, -(C_1-C_6 alkylenyl)-$S(O)_2R^m$, -(C_1-C_6 alkylenyl)-$S(O)_2N(R^m)_2$, -(C_1-C_6 alkylenyl)-$C(O)R^m$, -(C_1-C_6 alkylenyl)-$C(O)OR^m$, -(C_1-C_6 alkylenyl)-$C(O)N(R^m)_2$, -(C_1-C_6 alkylenyl)-$C(O)N(R^m)S(O)_2R^n$, -(C_1-C_6 alkylenyl)-$N(R^m)_2$, -(C_1-C_6 alkylenyl)-$N(R^m)C(O)R^n$, -(C_1-C_6 alkylenyl)-$N(R^m)S(O)_2R^n$, -(C_1-C_6 alkylenyl)-$N(R^m)C(O)O(R^n)$, -(C_1-C_6 alkylenyl)-$N(R^m)C(O)N(R^m)_2$, or -(C_1-C_6 alkylenyl)-$N(R^m)S(O)_2N(R^m)_2$;

R^h, at each occurrence, is independently hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, or -(C_1-C_6 alkylenyl)-OR^m;

R^{1a}, R^{1b}, R^{2a}, and R^{5b}, at each occurrence, are each independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, C_1-C_6 haloalkyl, oxo, -CN, -NO_2, -OR^m, -$OC(O)R^n$, -$OC(O)N(R^m)_2$, -SR^m, -$S(O)_2R^m$, -$S(O)_2N(R^m)_2$, -$C(O)R^m$, -$C(O)OR^m$, -C(O)O(benzyl), -$C(O)N(R^m)_2$, -$C(O)N(R^m)S(O)_2R^n$, -$N(R^m)_2$, -$N(R^m)$(alkoxyalkyl), -N(alkoxyalkyl)$_2$, -$N(R^m)C(O)R^n$, -$N(R^m)S(O)_2R^n$, -$N(R^m)C(O)O(R^n)$, -$N(R^m)C(O)N(R^m)_2$, -$N(R^m)S(O)_2N(R^m)_2$, -(C_1-C_6 alkylenyl)-CN, -(C_1-C_6 alkylenyl)-OR^m, -(C_1-C_6 alkylenyl)-$OC(O)R^n$, -(C_1-C_6 alkylenyl)-$OC(O)N(R^m)_2$, -(C_1-C_6 alkylenyl)-SR^m, -(C_1-C_6 alkylenyl)-$S(O)_2R^m$, -(C_1-C_6 alkylenyl)-$S(O)_2N(R^m)_2$, -(C_1-C_6 alkylenyl)-$C(O)R^m$, -(C_1-C_6 alkylenyl)-$C(O)OR^m$, -(C_1-C_6 alkylenyl)-$C(O)N(R^m)_2$, -(C_1-C_6 alkylenyl)-$C(O)N(R^m)S(O)_2R^n$, -(C_1-C_6 alkylenyl)-$N(R^m)_2$, -(C_1-C_6 alkylenyl)-$N(R^m)C(O)R^n$, -(C_1-C_6 alkylenyl)-$N(R^m)S(O)_2R^n$, -(C_1-C_6 alkylenyl)-$N(R^m)C(O)O(R^n)$, -(C_1-C_6 alkylenyl)-$N(R^m)C(O)N(R^n)_2$, or -(C_1-C_6 alkylenyl)-$N(R^m)S(O)_2N(R^n)_2$;

R^m, at each occurrence, is independently hydrogen, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

R^n, at each occurrence, is independently C_1-C_6 alkyl or C_1-C_6 haloalkyl; and

R^6 is hydrogen.

[00245] Exemplary compounds of formula (I) include, but are not limited to:

N-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(benzenesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-methyl-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-*N*-(trifluoromethanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(cyclopropanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1-[3-(trifluoromethoxy)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-1-phenyl-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-[2-(dimethylamino)pyrimidin-5-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(azetidin-1-yl)phenyl]-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-[2-(morpholin-4-yl)pyrimidin-5-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-*tert*-butyl-1-cyclopentyl-*N*-(methanesulfonyl)-4-[6-(morpholin-4-yl)pyridin-3-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-3-methyl-1-phenyl-4-(piperidin-1-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-(4-methoxyphenyl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-4-(4-methoxyphenyl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1-[3-(pyrrolidin-1-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-1-(6-methoxypyridin-3-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(3-chloro-4-methylphenyl)-*N*-(methanesulfonyl)-4-(4-methoxyphenyl)-3-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-3-methyl-1-phenyl-4-(piperidin-1-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[2-(morpholin-4-yl)pyrimidin-5-yl]-1-phenyl-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(2,4-difluorophenyl)-*N*-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-[6-(dimethylamino)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(3,5-difluorophenyl)-*N*-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(3,5-dimethylphenyl)-*N*-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(3,4-difluorophenyl)-*N*-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-3-methyl-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-(4-methoxyphenyl)-3-methyl-1-(3-methylphenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-4-(4-methoxyphenyl)-3-methyl-1-(3-methylphenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[2-(dimethylamino)pyrimidin-5-yl]-*N*-(methanesulfonyl)-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[2-(dimethylamino)pyrimidin-5-yl]-*N*-(ethanesulfonyl)-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(dimethylamino)pyridin-3-yl]-*N*-(methanesulfonyl)-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(dimethylamino)pyridin-3-yl]-*N*-(ethanesulfonyl)-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[6-(morpholin-4-yl)pyridin-3-yl]-1-phenyl-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-4-[6-(morpholin-4-yl)pyridin-3-yl]-1-phenyl-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-1-[3-(3-methoxyazetidin-1-yl)phenyl]-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-3-methyl-4-[6-(morpholin-4-yl)pyridin-3-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4,4-difluorocyclohexyl)-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-(oxan-3-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-(oxan-3-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-{4-[3-(dimethylamino)azetidin-1-yl]phenyl}-*N*-(methanesulfonyl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-{4-[3-(dimethylamino)azetidin-1-yl]phenyl}-*N*-(ethanesulfonyl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(3,3-dimethylazetidin-1-yl)phenyl]-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-[6-(morpholin-4-yl)pyridin-3-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(ethanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(3-fluoropyrrolidin-1-yl)phenyl]-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-3-methyl-4-[6-(morpholin-4-yl)pyridin-3-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(ethanesulfonyl)-3-methyl-4-[6-(morpholin-4-yl)pyridin-3-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-[2-(dimethylamino)pyrimidin-5-yl]-*N*-(methanesulfonyl)-3-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-[2-(dimethylamino)pyrimidin-5-yl]-*N*-(ethanesulfonyl)-3-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-{6-[methyl(oxan-4-yl)amino]pyridin-3-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

methyl 3-{1-cyclohexyl-4-[2-(dimethylamino)pyrimidin-5-yl]-6-[(ethanesulfonyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-3-yl}azetidine-1-carboxylate;

1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-[6-(morpholin-4-yl)pyridin-3-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(dimethylamino)phenyl]-*N*-(ethanesulfonyl)-4-[6-(morpholin-4-yl)pyridin-3-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclopentyl-4-[6-(dimethylamino)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclopentyl-4-[6-(dimethylamino)pyridin-3-yl]-*N*-(ethanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-3-methyl-4-[6-(morpholin-4-yl)pyridin-3-yl]-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-3-methyl-4-[6-(morpholin-4-yl)pyridin-3-yl]-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-[2-(morpholin-4-yl)pyrimidin-5-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(2,4-difluorophenyl)-*N*-(methanesulfonyl)-3-methyl-4-[6-(morpholin-4-yl)pyridin-3-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(2,4-difluorophenyl)-*N*-(ethanesulfonyl)-3-methyl-4-[6-(morpholin-4-yl)pyridin-3-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(dimethylamino)phenyl]-*N*-(ethanesulfonyl)-4-[2-(morpholin-4-yl)pyrimidin-5-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-{6-[(2-methoxyethyl)(methyl)amino]pyridin-3-yl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-[6-(3,3-difluoropyrrolidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(3-chlorophenyl)-*N*-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(3-chlorophenyl)-*N*-(ethanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(3-fluorophenyl)-*N*-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-1-(3-fluorophenyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1-[4-(trifluoromethoxy)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1-[4-(trifluoromethoxy)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-1-(3-methoxyphenyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-1-(3-methoxyphenyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-{6-[methyl(oxan-4-yl)amino]pyridin-3-yl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-{4-[(2-methoxyethyl)(methyl)amino]phenyl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-1-{3-[(2-methoxyethyl)(methyl)amino]phenyl}-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(dimethylamino)phenyl]-4-[2-(dimethylamino)pyrimidin-5-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(dimethylamino)phenyl]-4-[2-(dimethylamino)pyrimidin-5-yl]-*N*-(ethanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(4-acetamidophenyl)-1-cyclohexyl-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(4-cyanopiperidin-1-yl)phenyl]-1-cyclohexyl-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(4-cyanopiperidin-1-yl)phenyl]-1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-{4-[(2-methoxyethyl)(methyl)amino]phenyl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-{6-[(2-methoxyethyl)(methyl)amino]pyridin-3-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-{6-[(2-methoxyethyl)(methyl)amino]pyridin-3-yl}-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-{6-[methyl(oxan-4-yl)amino]pyridin-3-yl}-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-{4-[(2-methoxyethyl)(methyl)amino]phenyl}-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-{6-[methyl(oxan-4-yl)amino]pyridin-3-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(ethanesulfonyl)-4-{6-[methyl(oxan-4-yl)amino]pyridin-3-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-{2-[methyl(oxan-4-yl)amino]pyrimidin-5-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-3-cyclopropyl-4-[6-(dimethylamino)pyridin-3-yl]-*N*-(ethanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-[6-(2,6-dimethylmorpholin-4-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-[6-(2,2-dimethylmorpholin-4-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[2-(4-cyanopiperidin-1-yl)pyrimidin-5-yl]-1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-{4-[methyl(oxan-4-yl)amino]phenyl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-{4-[methyl(oxan-4-yl)amino]phenyl}-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyano-4-methylpiperidin-1-yl)pyridin-3-yl]-1-cyclohexyl-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[2-(4-cyanopiperidin-1-yl)pyrimidin-5-yl]-*N*-(methanesulfonyl)-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-{4-[3-(dimethylamino)pyrrolidin-1-yl]phenyl}-*N*-(methanesulfonyl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-1-(3-methylphenyl)-4-(piperidin-1-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-1-(3-methylphenyl)-4-(piperidin-1-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(4-cyanopiperidin-1-yl)phenyl]-3-cyclobutyl-1-cyclohexyl-*N*-(methanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-cyclobutyl-1-cyclohexyl-*N*-(methanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(3-hydroxyazetidin-1-yl)phenyl]-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-[6-(3-methoxypyrrolidin-1-yl)pyridin-3-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

methyl 3-{4-(4-acetamidophenyl)-1-(3,5-difluorophenyl)-6-[(methanesulfonyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-3-yl}azetidine-1-carboxylate;

1-cyclohexyl-4-[6-(3-fluoropiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-{4-[(2-methoxyethyl)(methyl)amino]phenyl}-3-(propan-2-yl)-1-[3-(pyrrolidin-1-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-{4-[methyl(oxan-4-yl)amino]phenyl}-3-(propan-2-yl)-1-[3-(pyrrolidin-1-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-{4-[methyl(oxan-4-yl)amino]phenyl}-1-[3-(pyrrolidin-1-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-4-[2-(morpholin-4-yl)pyrimidin-5-yl]-1-phenyl-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(2,4-difluorophenyl)-*N*-(ethanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(3-chloro-4-methylphenyl)-*N*-(ethanesulfonyl)-4-(4-methoxyphenyl)-3-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(3,5-dimethylphenyl)-*N*-(ethanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(3,4-difluorophenyl)-*N*-(ethanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-(4-methoxypiperidin-1-yl)-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-4-(4-methoxypiperidin-1-yl)-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[2-(4-cyanopiperidin-1-yl)pyrimidin-5-yl]-1-cyclohexyl-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-{2-[(2-methoxyethyl)(methyl)amino]pyrimidin-5-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-{6-[bis(2-methoxyethyl)amino]pyridin-3-yl}-1-cyclohexyl-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-{6-[methyl(oxolan-3-yl)amino]pyridin-3-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-{2-[methyl(oxan-4-yl)amino]pyrimidin-5-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[6-(dimethylamino)pyridin-2-yl]-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1-[3-(trifluoromethoxy)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(3,4-difluorophenyl)-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-[6-(morpholin-4-yl)pyridin-2-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(2,6-difluoro-4-methoxyphenyl)-1-(3-fluoro-5-methoxyphenyl)-*N*-(methanesulfonyl)-3-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(4-cyanopiperidin-1-yl)phenyl]-1-(3,5-difluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(4-cyanopiperidin-1-yl)phenyl]-1-(3-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-{4-[(2-methoxyethyl)(methyl)amino]phenyl}-3-(propan-2-yl)-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-{6-[methyl(oxan-4-yl)amino]pyridin-3-yl}-3-(propan-2-yl)-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-{2-[methyl(oxan-4-yl)amino]pyrimidin-5-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(4-cyanopiperidin-1-yl)phenyl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-[2-(morpholin-4-yl)pyridin-4-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-3-(1-methylcyclobutyl)-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-3-(1-methylcyclobutyl)-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[2-(4-cyanopiperidin-1-yl)pyrimidin-5-yl]-1-(2,4-difluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-1-(2,4-difluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(4-cyanopiperidin-1-yl)phenyl]-1-(2,4-difluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-(4-methoxypiperidin-1-yl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(1,1-dioxo-1λ^6-thiolane-3-sulfonyl)-4-(4-methoxypiperidin-1-yl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-1-(oxan-3-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(2-methoxyethanesulfonyl)-4-(4-methoxypiperidin-1-yl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-(4-methoxypiperidin-1-yl)-1-phenyl-*N*-(3,3,3-trifluoropropane-1-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(1,1-difluoro-5-azaspiro[2.4]heptan-5-yl)-*N*-(methanesulfonyl)-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-(4-methoxypiperidin-1-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-4-{4-[(propan-2-yl)oxy]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-4-(4-propoxypiperidin-1-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[3-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-{4-[2-oxo-2-(pyrrolidin-1-yl)ethoxy]piperidin-1-yl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-(4-methoxypiperidin-1-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-(piperidin-1-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1-[2-(pyrrolidin-1-yl)pyridin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-(1-oxa-7-azaspiro[3.5]nonan-7-yl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(4-cyanopiperidin-1-yl)-1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[4-(2-methoxyethyl)piperidin-1-yl]-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-(3-methoxypiperidin-1-yl)-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-4-(3-methoxypiperidin-1-yl)-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(fluoromethyl)piperidin-1-yl]-*N*-(methanesulfonyl)-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[4-(methanesulfonyl)piperidin-1-yl]-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(4-methoxypiperidin-1-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(4-cyanopiperidin-1-yl)phenyl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1-[2-(pyrrolidin-1-yl)pyridin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[(2-methoxyethyl)(methyl)amino]-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-1-(3-methylphenyl)-4-(8-oxa-2-azaspiro[4.5]decan-2-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(4-butoxypiperidin-1-yl)-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(4-methoxy-4-methylpiperidin-1-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

2-[(2-{[3-cyclobutyl-4-(4-methoxypiperidin-1-yl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl]sulfamoyl}ethyl)carbamoyl]benzoic acid;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[4-(2-methylpropoxy)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-(4-methoxypiperidin-1-yl)-1-phenyl-*N*-(2,2,2-trifluoroethanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(1-oxa-7-azaspiro[3.5]nonan-7-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[3-(difluoromethyl)piperidin-1-yl]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(6-oxa-2-azaspiro[3.5]nonan-2-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(1-oxa-8-azaspiro[4.5]decan-8-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-(cyclohexylmethoxy)-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-4-(piperidin-1-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(2-methoxyethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(2-azaspiro[3.4]octan-2-yl)-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(3-azabicyclo[3.1.0]hexan-3-yl)-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-(4-methoxypiperidin-1-yl)-1-[2-(morpholin-4-yl)pyridin-4-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-(4-methoxypiperidin-1-yl)-3-(propan-2-yl)-1-[2-(pyrrolidin-1-yl)pyridin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-cyclobutyl-*N*-(methanesulfonyl)-1-[2-(pyrrolidin-1-yl)pyridin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(methanesulfonyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(4-cyanopiperidin-1-yl)-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(2-azaspiro[3.5]nonan-2-yl)-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[3-(methoxymethyl)azetidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(*cis*-3-methoxycyclobutyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-(3,3-difluorocyclobutyl)-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-(3,3-dimethylcyclobutyl)-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-(3-fluorocyclobutyl)-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[2-(oxan-4-yl)ethoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[(2*S*)-2-fluoro-2-(oxan-4-yl)ethoxy]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-cyclobutyl-*N*-(methanesulfonyl)-1-[2-(morpholin-4-yl)pyridin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-(1,1-difluoro-5-azaspiro[2.4]heptan-5-yl)-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-(5-oxa-2-azaspiro[3.5]nonan-2-yl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-(7-oxa-2-azaspiro[3.5]nonan-2-yl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(5-azaspiro[2.5]octan-5-yl)-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[(2-methoxyethyl)(methyl)amino]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-(4-methoxypiperidin-1-yl)-*N*-(oxane-4-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

benzyl 4-{[3-cyclobutyl-4-(4-methoxypiperidin-1-yl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl]sulfamoyl}piperidine-1-carboxylate;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-(*cis*-3-fluorocyclobutyl)-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-(*trans*-3-fluorocyclobutyl)-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[(*cis*-4-methoxycyclohexyl)oxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[(*trans*-4-methoxycyclohexyl)oxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-{4-[(benzyloxy)methyl]piperidin-1-yl}-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(2-azaspiro[3.3]heptan-2-yl)-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

methyl 5-{3-cyclobutyl-6-[(methanesulfonyl)carbamoyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}octahydro-1*H*-pyrrolo[3,2-*c*]pyridine-1-carboxylate;

4-(1-acetyloctahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl)-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-(4-methoxypiperidin-1-yl)-1-[6-(morpholin-4-yl)pyridin-2-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-{4-[(1*S*)-2-(dimethylamino)-1-fluoroethyl]piperidin-1-yl}-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(fluoromethyl)piperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[4-(2-methoxypropan-2-yl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(3-azaspiro[5.5]undecan-3-yl)-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(3,4-difluorophenyl)-*N*-(ethanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-1-(3-fluorophenyl)-4-{6-[methyl(oxan-4-yl)amino]pyridin-3-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(cyclopropanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(2-methoxyethanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-1-[2-(morpholin-4-yl)pyridin-4-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(cyclopentyloxy)piperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(cyclohexyloxy)piperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(cyclopropylmethoxy)piperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(2-methoxyethanesulfonyl)-4-(4-methoxyphenyl)-3-methyl-1-(2-methylpropyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(2-methoxyethanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-(oxolan-3-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(2-methoxyethanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(2-methoxyethanesulfonyl)-4-(4-methoxyphenyl)-3-methyl-1-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclopropyl-*N*-(2-methoxyethanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(2-methoxyethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[(2*R*)-2-fluoro-2-(oxan-4-yl)ethoxy]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[(3,3-difluorocyclopentyl)methoxy]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(cyclopropanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(4-cyanopiperidin-1-yl)-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(1-methoxyethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-4-[4-(1,1,1-trifluoro-2-methoxypropan-2-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[2-(1,1-dioxo-1λ^6,4-thiazinan-4-yl)ethoxy]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(hydroxymethyl)piperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-(1-methyl-1*H*-pyrazole-4-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-{6-[bis(2-methoxyethyl)amino]pyridin-3-yl}-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-methoxy-4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-[2-(morpholin-4-yl)pyridin-4-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(2-methoxyethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-[2-(morpholin-4-yl)pyridin-4-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(1,2-dimethyl-1*H*-imidazole-4-sulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(2-methoxyethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-{6-[bis(2-methoxyethyl)amino]pyridin-3-yl}-*N*-(methanesulfonyl)-1-[2-(morpholin-4-yl)pyridin-4-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-*N*-(1*H*-pyrazole-4-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[(3-methyloxetan-3-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-{4-[(1,1-dioxo-1λ^6,4-thiazinan-4-yl)methyl]-4-methoxypiperidin-1-yl}-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(2-methoxyethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(*trans*-3-methylcyclobutyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-1-phenyl-3-[(piperidin-4-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

tert-butyl 4-({4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-6-[(methanesulfonyl)carbamoyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-3-yl}oxy)piperidine-1-carboxylate;

3-cyclobutyl-*N*-[2-(1,3-dioxo-1,3-dihydro-2*H*-isoindol-2-yl)ethanesulfonyl]-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(2-aminoethanesulfonyl)-3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(cyclobutylmethyl)-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(cyclobutylmethyl)-*N*-(2-methoxyethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-(2-methylpropyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(2-methoxyethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-(2-methylpropyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-4-[4-(2,2,2-trifluoroethyl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[2-(morpholin-4-yl)ethanesulfonyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-(1-methyl-6-oxo-1,6-dihydropyridazin-3-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(2-methoxyethanesulfonyl)-4-[(3-methyloxetan-3-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-4-[4-(propan-2-yl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(2-methoxyethanesulfonyl)-1-phenyl-4-[4-(propan-2-yl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[3-(morpholin-4-yl)propane-1-sulfonyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-[2-(dimethylamino)ethanesulfonyl]-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[(1-acetyl-4-fluoropiperidin-4-yl)methoxy]-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(2-methoxyethanesulfonyl)-3-[(oxolan-3-yl)oxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(2-methoxyethanesulfonyl)-3-(*trans*-3-methylcyclobutyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-[(oxolan-3-yl)oxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-[(oxan-4-yl)methoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-[2-(morpholin-4-yl)pyrimidin-4-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(4-cyclobutylpiperazin-1-yl)-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[3-(morpholin-4-yl)propoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[(3,3-difluoro-1-methylcyclobutyl)methoxy]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[(oxolan-2-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[(oxan-4-yl)methoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[2-(oxan-4-yl)ethoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-(1-methyl-1*H*-imidazole-4-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(3,5-dimethyl-1,2-oxazole-4-sulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

methyl 3-({3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)propanoate;

3-({3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)propanoic acid;

N-[3-(dimethylamino)propane-1-sulfonyl]-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-*N*-[3-(pyrrolidin-1-yl)propane-1-sulfonyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[3-(morpholin-4-yl)propoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[(3-methyloxetan-3-yl)methoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(2-methoxypropan-2-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[(oxolan-2-yl)methoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[(1-acetylpiperidin-4-yl)methoxy]-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

methyl 4-[({3-cyclobutyl-6-[(methanesulfonyl)carbamoyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}oxy)methyl]piperidine-1-carboxylate;

3-cyclobutyl-*N*-[3-(dimethylamino)-3-oxopropane-1-sulfonyl]-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[3-(dimethylamino)propoxy]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-[(oxetan-3-yl)oxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[(2-methoxyethyl)(methyl)amino]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-[3-(azetidin-1-yl)propane-1-sulfonyl]-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[3-(dimethylamino)propoxy]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-4-[4-(2-hydroxypropan-2-yl)piperidin-1-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[2-(1-methylpiperidin-2-yl)ethoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[(3,3-difluoro-1-methylcyclobutyl)methoxy]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[3-(piperidin-1-yl)propoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[(1-acetyl-4-fluoropiperidin-4-yl)methoxy]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-{2-[(oxetan-3-yl)(propan-2-yl)amino]ethoxy}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-4-{[4-(propan-2-yl)morpholin-3-yl]methoxy}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[(1,3-dimethoxypropan-2-yl)oxy]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[(1,4-dioxan-2-yl)methoxy]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-{2-[(oxetan-3-yl)oxy]ethoxy}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-4-[3-(piperidin-1-yl)propoxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(2-methoxyethanesulfonyl)-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(2-hydroxypropan-2-yl)piperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[(oxan-4-yl)methoxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(dimethylamino)piperidin-1-yl]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(1'-methyl[4,4'-*b*ipiperidin]-1-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[(1-acetylpiperidin-4-yl)methoxy]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

methyl 4-({[1-(4-fluorophenyl)-6-[(methanesulfonyl)carbamoyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl]oxy}methyl)piperidine-1-carboxylate;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[2-(1-methylpiperidin-2-yl)ethoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[(1,3-dimethoxypropan-2-yl)oxy]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-{2-[(oxetan-3-yl)(propan-2-yl)amino]ethoxy}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(cyanomethyl)-4-hydroxypiperidin-1-yl]-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(4-azidophenyl)-*N*-(3-azidopropane-1-sulfonyl)-1-[3-(dimethylamino)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-4-[4-(2,2,2-trifluoroethyl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(2-methoxyethanesulfonyl)-1-phenyl-4-[4-(2,2,2-trifluoroethyl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-{4-[2-(morpholin-4-yl)ethyl]piperidin-1-yl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

rac-4-[(3a*R*,7a*S*)-1-acetyloctahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl]-3-cyclobutyl-*N*-[3-(morpholin-4-yl)propane-1-sulfonyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(cyclopropanesulfonyl)-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(ethanesulfonyl)-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-1-[2-(morpholin-4-yl)pyridin-4-yl]-4-[(oxan-4-yl)methoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

ethyl 4-[1-(4-fluorophenyl)-6-[(methanesulfonyl)carbamoyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl]piperazine-1-carboxylate;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(3-methyl-2-oxo-1-oxa-3,8-diazaspiro[4.5]decan-8-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-4-[3-(trifluoromethyl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[4-(2-methoxyethyl)piperazin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(2,4-dioxo-1,3,8-triazaspiro[4.5]decan-8-yl)-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(ethoxymethyl)-4-fluoropiperidin-1-yl]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-{4-fluoro-4-[(2-methoxyethoxy)methyl]piperidin-1-yl}-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[(3*R*,4*R*)-3-fluoro-4-hydroxypiperidin-1-yl]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-fluoro-4-(methoxymethyl)piperidin-1-yl]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-{3-fluoro-3-[(2-methoxyethoxy)methyl]piperidin-1-yl}-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-[3-(morpholin-4-yl)propane-1-sulfonyl]-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-([1,4'-*b*ipiperidin]-1'-yl)-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[(3*R*)-3-(hydroxymethyl)piperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[(3*R*)-3-(hydroxymethyl)piperidin-1-yl]-*N*-[3-(morpholin-4-yl)propane-1-sulfonyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[(oxan-4-yl)methoxy]-1-phenyl-*N*-[4-(pyrrolidin-1-yl)piperidine-1-sulfonyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-[(2*S*)-2-(4-methylpiperazine-1-carbonyl)pyrrolidine-1-sulfonyl]-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-([1,4'-*b*ipiperidine]-1'-sulfonyl)-3-cyclobutyl-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-[methyl(propyl)sulfamoyl]-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-[ethyl(propyl)sulfamoyl]-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

ethyl 4-[({3-cyclobutyl-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)amino]piperidine-1-carboxylate;

N-(4-acetyl-1,4-diazepane-1-sulfonyl)-3-cyclobutyl-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(morpholine-4-sulfonyl)-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-[4-(morpholin-4-yl)piperidine-1-sulfonyl]-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-[4-(4-methylpiperazine-1-carbonyl)piperidine-1-sulfonyl]-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(4-methylpiperazine-1-sulfonyl)-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(2-methylpropane-2-sulfonyl)-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(4-azidophenyl)-*N*-(but-3-yne-1-sulfonyl)-1-[3-(dimethylamino)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(cyanomethanesulfonyl)-3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-([1,4'-*b*ipiperidin]-1'-yl)-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(2-hydroxyethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(3-hydroxypropane-1-sulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-*N*-(piperidine-4-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-(oxolane-3-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(2,6-dimethylpyridin-4-yl)-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-(1,1-dioxo-1λ^6,4-thiazinan-4-yl)-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-*N*-[2-(1*H*-pyrazol-1-yl)ethanesulfonyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

benzyl [2-({3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)ethyl]carbamate;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-(1-methylcyclopropane-1-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-(2-methylpropane-1-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

methyl ({3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)acetate;

benzyl 3-({3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)pyrrolidine-1-carboxylate;

tert-butyl 4-[1-(4-fluorophenyl)-6-[(methanesulfonyl)carbamoyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl]piperidine-1-carboxylate;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[2-(methoxymethyl)morpholin-4-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(morpholine-4-sulfonyl)-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[4-(propan-2-yl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(morpholine-4-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(2-amino-2-oxoethanesulfonyl)-3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-(2-methoxypyridin-4-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(2-acetamidoethanesulfonyl)-3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-*N*-(pyrrolidine-3-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-*N*-[4-(pyrrolidin-1-yl)piperidine-1-sulfonyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[(2*S*)-2-(4-methylpiperazine-1-carbonyl)pyrrolidine-1-sulfonyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-{4-[(2*S*)-2-(methoxymethyl)pyrrolidin-1-yl]piperidine-1-sulfonyl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[methyl(propyl)sulfamoyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-[ethyl(propyl)sulfamoyl]-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

ethyl 4-[({3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)amino]piperidine-1-carboxylate;

N-(4-acetyl-1,4-diazepane-1-sulfonyl)-3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-{4-[(2*R*)-2-(methoxymethyl)pyrrolidin-1-yl]piperidine-1-sulfonyl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-(morpholine-4-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[4-(morpholin-4-yl)piperidine-1-sulfonyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[4-(4-methylpiperazine-1-carbonyl)piperidine-1-sulfonyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(4-fluoropiperidine-1-sulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-(4-methylpiperazine-1-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(cyclopropanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(ethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-{4-[(morpholin-4-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(2-methoxyethanesulfonyl)-4-{4-[(morpholin-4-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[(morpholin-4-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(2-methoxyethanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[(morpholin-4-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-{4-[(morpholin-4-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(cyclopropanesulfonyl)-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(2-methoxyethanesulfonyl)-4-{4-[2-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[2-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-[(1,4-dioxan-2-yl)methanesulfonyl]-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(2-methoxyethanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-[4-(4-methylpiperazine-1-carbonyl)phenyl]-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-[4-(4-methylpiperazine-1-carbonyl)phenyl]-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[(morpholin-4-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[2-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-*N*-(ethanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-*N*-(cyclopropanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-*N*-(oxolane-3-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-(2-methylpyridin-4-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-{4-[2-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-[methyl(propyl)sulfamoyl]-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

ethyl 4-[({3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)amino]piperidine-1-carboxylate;

3-cyclobutyl-*N*-(4-fluoropiperidine-1-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(1-methylcyclopropane-1-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(cyclopropanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(ethanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(2-methoxyethanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-{4-[(2*S*)-2-(methoxymethyl)pyrrolidin-1-yl]piperidine-1-sulfonyl}-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[1-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-{4-[(4-methylpiperazin-1-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[(4-methylpiperazin-1-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[(piperidin-1-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(dimethylsulfamoyl)-3-[(propan-2-yl)oxy]-4-{4-[(pyrrolidin-1-yl)methyl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-{4-[1-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(ethanesulfonyl)-1-(4-fluorophenyl)-4-{4-[1-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(2-methoxyethanesulfonyl)-4-{4-[(morpholin-4-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(2-hydroxyethanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(chloromethanesulfonyl)-3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-1-(4-fluorophenyl)-*N*-(oxolane-3-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[2-(morpholin-4-yl)ethyl]piperidin-1-yl}-*N*-(oxolane-3-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-([1,4'-bipiperidine]-1'-sulfonyl)-3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-*N*-[3-(morpholin-4-yl)propane-1-sulfonyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(4-methylpiperazine-1-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

ethyl 4-{[(3-cyclobutyl-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl)sulfamoyl]amino}piperidine-1-carboxylate;

3-cyclobutyl-*N*-{4-[(2*R*)-2-(methoxymethyl)pyrrolidin-1-yl]piperidine-1-sulfonyl}-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(4-fluoropiperidine-1-sulfonyl)-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(4-methylpiperazine-1-sulfonyl)-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(1-methylcyclopropane-1-sulfonyl)-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(cyclopropanesulfonyl)-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(ethanesulfonyl)-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(2-methoxyethanesulfonyl)-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(2-methylpropane-2-sulfonyl)-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(ethanesulfonyl)-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-(cyclobutyloxy)-1-cyclohexyl-4-{4-[(morpholin-4-yl)methyl]phenyl}-*N*-(oxolane-3-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(oxolane-3-sulfonyl)-4-[4-(pyridin-4-yl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-[4-(pyridin-4-yl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(ethanesulfonyl)-4-[4-(pyridin-4-yl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-[(2-methoxyethyl)(methyl)sulfamoyl]-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-[2-(oxan-4-yl)pyridin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-1-(2-methoxypyridin-4-yl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[(morpholin-4-yl)methyl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[2-(morpholin-4-yl)ethyl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(but-3-yne-1-sulfonyl)-3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-*N*-(ethanesulfonyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[(1*R*)-1-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[(1*S*)-1-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-(cyclobutyloxy)-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[(morpholin-4-yl)methyl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-[methyl(propan-2-yl)sulfamoyl]-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-[ethyl(methyl)sulfamoyl]-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(3-methoxyazetidine-1-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-*N*-(pyrrolidine-1-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-*N*-(2,2,2-trifluoroethanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(morpholine-4-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-1-(4-fluorophenyl)-*N*-(2-methoxyethanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(dimethylsulfamoyl)-1-[2-(morpholin-4-yl)pyridin-4-yl]-4-[(oxan-4-yl)methoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-[2-(oxan-4-yl)pyridin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(2-hydroxyethanesulfonyl)-4-{4-[2-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

methyl 4-(1-{3-cyclobutyl-6-[(dimethylsulfamoyl)carbamoyl]-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperidin-4-yl)piperazine-1-carboxylate;

4-[4-(4-acetylpiperazin-1-yl)piperidin-1-yl]-3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(ethanesulfonyl)-1-(4-fluorophenyl)-4-{4-[(morpholin-4-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[(morpholin-4-yl)methyl]piperidin-1-yl}-*N*-(oxolane-3-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

ethyl 4-[1-(4-fluorophenyl)-6-[(methanesulfonyl)carbamoyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl]piperidine-1-carboxylate;

ethyl 4-{6-[(dimethylsulfamoyl)carbamoyl]-1-(4-fluorophenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperidine-1-carboxylate;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(3-methylphenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(3-methoxyphenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-[4-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(ethoxymethyl)-4-fluoropiperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-{4-fluoro-4-[(2-methoxyethoxy)methyl]piperidin-1-yl}-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-{3-fluoro-3-[(2-methoxyethoxy)methyl]piperidin-1-yl}-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-fluoro-4-(methoxymethyl)piperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(4-cyanopiperidine-1-sulfonyl)-3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-*N*-(oxetane-3-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(cyclopropanesulfonyl)-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(1-methylcyclopropane-1-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-1-(3-methylphenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-[4-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluoro-3-methylphenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(3-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluoro-3-methylphenyl)-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(3-fluorophenyl)-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[(4-methylpiperazin-1-yl)methyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[(morpholin-4-yl)methyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[(morpholin-4-yl)methyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{[4-(methoxymethyl)piperidin-1-yl]methyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(4-cyano[1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(3-cyanoazetidin-1-yl)piperidin-1-yl]-3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[4-(3-methoxypyrrolidin-1-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-(4-fluoro[1,4'-bipiperidin]-1'-yl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-(4,4-difluoro[1,4'-bipiperidin]-1'-yl)-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(2-cyanomorpholin-4-yl)piperidin-1-yl]-3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[methyl(oxan-4-yl)amino]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-{2-[(propan-2-yl)oxy]pyridin-4-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-{2-[(propan-2-yl)oxy]pyridin-4-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-[2-(oxan-4-yl)pyridin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[4-(2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[3-(morpholin-4-yl)-1-oxa-8-azaspiro[4.5]decan-8-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(dimethylsulfamoyl)-3-[(propan-2-yl)oxy]-4-{4-[4-(propan-2-yl)piperazin-1-yl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-[4-(2-methylpyridin-4-yl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-4-[6-(4-cyclopropylpiperazin-1-yl)pyridin-3-yl]-*N*-(dimethylsulfamoyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(3-fluoropyrrolidine-1-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(3-methoxypyrrolidine-1-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-[4-(methoxymethyl)piperidine-1-sulfonyl]-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[4-(3-fluoropyrrolidin-1-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{6-[4-(propan-2-yl)piperazin-1-yl]pyridin-3-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[1-(morpholin-4-yl)ethyl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-{4-[4-(dimethylamino)piperidine-1-carbonyl]phenyl}-*N*-(methanesulfonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-{4-[4-(dimethylamino)piperidine-1-carbonyl]phenyl}-*N*-(2-methoxyethanesulfonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-{4-[4-(dimethylamino)piperidine-1-carbonyl]phenyl}-*N*-(dimethylsulfamoyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[4-(propan-2-yl)piperazin-1-yl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-*N*-(dimethylsulfamoyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(cyclopropanesulfonyl)-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-[6-(4-methylpiperazin-1-yl)pyridin-3-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{6-[4-(2-methoxyethyl)piperazin-1-yl]pyridin-3-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[4-(propan-2-yl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-*N*-[methyl(propyl)sulfamoyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-*N*-(morpholine-4-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-*N*-(1-methylcyclopropane-1-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-*N*-(methylsulfamoyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-[4-(4-cyclopropylpiperazin-1-yl)phenyl]-*N*-(dimethylsulfamoyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[3-(trifluoromethyl)pyrrolidin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(3-cyanopyrrolidin-1-yl)piperidin-1-yl]-3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(3-cyano[1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-(3-fluoro[1,4'-bipiperidin]-1'-yl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-{4-[3-(trifluoromethyl)pyrrolidin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(3-cyanopyrrolidin-1-yl)piperidin-1-yl]-3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(3-cyano[1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-(3-fluoro[1,4'-bipiperidin]-1'-yl)-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-*N*-(piperidine-1-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(3-fluoroazetidine-1-sulfonyl)-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[4-(3-methoxyazetidin-1-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[3-(trifluoromethyl)[1,4'-bipiperidin]-1'-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-(3-methoxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(2,2-dimethylmorpholin-4-yl)piperidin-1-yl]-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(2-acetamidoethanesulfonyl)-3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-[2-(difluoromethoxy)pyridin-4-yl]-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(azetidine-1-sulfonyl)-3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-[(2*R*)-2-(methoxymethyl)pyrrolidine-1-sulfonyl]-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-*N*-[(oxan-4-yl)sulfamoyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-[methyl(oxan-4-yl)sulfamoyl]-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(3,3-difluoroazetidine-1-sulfonyl)-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[(3*S*)-4-benzyl-3-methylpiperazin-1-yl]-3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[(3*R*)-4-benzyl-3-methylpiperazin-1-yl]-3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-(9-cyclopropyl-3,9-diazaspiro[5.5]undecan-3-yl)-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[4-(3-methoxyazetidin-1-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[3-(trifluoromethyl)[1,4'-bipiperidin]-1'-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(3-methoxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(2,2-dimethylmorpholin-4-yl)piperidin-1-yl]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

ethyl 4-(1-{3-cyclobutyl-6-[(dimethylsulfamoyl)carbamoyl]-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperidin-4-yl)piperazine-1-carboxylate;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[(2-methoxyethyl)(methyl)amino]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methoxysulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[1-(4,4-difluorocyclohexyl)piperidin-4-yl]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[1-(4,4-difluorocyclohexyl)piperidin-4-yl]-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{[4-(morpholin-4-yl)piperidin-1-yl]methyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-{[4-(morpholin-4-yl)piperidin-1-yl]methyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-{4-[(4-cyclopropylpiperazin-1-yl)methyl]phenyl}-*N*-(methanesulfonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[1-(propan-2-yl)piperidin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[1-(oxan-4-yl)piperidin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-{1-[(oxan-4-yl)methyl]piperidin-4-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{1-[(oxan-4-yl)methyl]piperidin-4-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-{1-[(2,5-dimethoxyoxolan-3-yl)methyl]piperidin-4-yl}-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[1-(3,3,3-trifluoropropyl)piperidin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[1-(3,3,3-trifluoropropyl)piperidin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-(4-hydroxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

methyl {3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamate;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[4-(2-methoxyethyl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[3-(morpholin-4-yl)pyrrolidine-1-sulfonyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(4-cyclopropylpiperazine-1-sulfonyl)-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-[4-(2-methoxyethyl)piperazine-1-sulfonyl]-4-[4-(methoxymethyl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[1-(propan-2-yl)piperidin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[1-(oxan-4-yl)piperidin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[1-(cyclopropylmethyl)piperidin-4-yl]-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[9-(oxetan-3-yl)-3,9-diazaspiro[5.5]undecan-3-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[4-(oxetan-3-yl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[(1-cyclopropylpiperidin-4-yl)methoxy]-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[(1-cyclobutylpiperidin-4-yl)methoxy]-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[(1-cyclohexylpiperidin-4-yl)methoxy]-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{[1-(oxan-4-yl)piperidin-4-yl]methoxy}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-{1-[(2,5-dimethoxyoxolan-3-yl)methyl]piperidin-4-yl}-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-{2-[(propan-2-yl)oxy]pyrimidin-4-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(2-ethoxypyrimidin-4-yl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(2,2-difluoro-2*H*-1,3-benzodioxol-5-yl)-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(4-methylpiperazine-1-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[1-(propan-2-yl)octahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-(1-cyclobutyloctahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl)-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[1-(oxetan-3-yl)octahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[1-(oxan-4-yl)octahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-*N*-(methylsulfamoyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-*N*-sulfamoyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-[4-(hexahydropyrrolo[3,4-*c*]pyrrole-2(1*H*)-carbonyl)phenyl]-*N*-(methanesulfonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(azetidine-1-sulfonyl)-3-cyclobutyl-1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-(4-{[3-(dimethylamino)azetidin-1-yl]methyl}phenyl)-*N*-(methanesulfonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-3-[(propan-2-yl)oxy]-4-(4-{[4-(propan-2-yl)piperazin-1-yl]methyl}phenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-{4-[(4-methoxypiperidin-1-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-{4-[(5-methylhexahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-[4-(5-methylhexahydropyrrolo[3,4-*c*]pyrrole-2(1*H*)-carbonyl)phenyl]-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methylsulfamoyl)-4-{4-[4-(propan-2-yl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(4-cyano-1-methylpiperidin-4-yl)phenyl]-1-cyclohexyl-*N*-(methanesulfonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-{4-[3-(dimethylamino)azetidine-1-carbonyl]phenyl}-*N*-(methanesulfonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-{4-[(8-methyl-2-oxa-5,8-diazaspiro[3.5]nonan-5-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-{4-[(4-ethylpiperazin-1-yl)methyl]phenyl}-*N*-(methanesulfonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-(4-{[4-(dimethylamino)piperidin-1-yl]methyl}phenyl)-*N*-(methanesulfonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(3-methoxyazetidine-1-sulfonyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(3-fluoroazetidine-1-sulfonyl)-1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-*N*-(morpholine-4-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)cyclohexyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)cyclohexyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-(4-fluoro[1,4'-bipiperidin]-1'-yl)-1-(4-fluorophenyl)-*N*-(methylsulfamoyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(azetidine-1-sulfonyl)-3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[4-(propan-2-yl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-[3-(difluoromethoxy)phenyl]-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-*N*-methyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-*N*-methyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(ethanesulfonyl)-*N*-methyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(ethanesulfonyl)-*N*-methyl-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

2-(3-cyclobutyl-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl)-6-methyl-1λ^6,2,6-thiadiazinane-1,1-dione;

2-(3-cyclobutyl-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl)-1λ^6,2-thiazolidine-1,1-dione;

3-cyclobutyl-*N*-(methanesulfonyl)-*N*-methyl-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

2-(3-cyclobutyl-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl)-1λ^6,2-thiazinane-1,1-dione;

2-{3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}-6-methyl-1λ^6,2,6-thiadiazinane-1,1-dione;

2-{3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}-1λ^6,2-thiazolidine-1,1-dione;

2-{3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}-1λ^6,2-thiazinane-1,1-dione;

2-{3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}-1λ^6,2-thiazolidine-1,1-dione;

2-{3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}-1λ^6,2-thiazinane-1,1-dione;

3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-(methylsulfamoyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(2-methoxyethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-(morpholine-4-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(3-hydroxypropane-1-sulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

ethyl 4-[({3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)amino]piperidine-1-carboxylate;

3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[(oxetan-3-yl)sulfamoyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[(oxan-4-yl)sulfamoyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[4-(morpholin-4-yl)piperidine-1-sulfonyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

ethyl 4-{3-cyclobutyl-1-(4-fluorophenyl)-6-[(2-methoxyethanesulfonyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperazine-1-carboxylate;

ethyl 4-{3-cyclobutyl-1-(4-fluorophenyl)-6-[(morpholine-4-sulfonyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperazine-1-carboxylate;

ethyl 4-{3-cyclobutyl-1-(4-fluorophenyl)-6-[(methanesulfonyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperazine-1-carboxylate;

ethyl 4-{3-cyclobutyl-1-(4-fluorophenyl)-6-[(methylsulfamoyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperazine-1-carboxylate;

2-methylpropyl 4-{3-cyclobutyl-1-(4-fluorophenyl)-6-[(methanesulfonyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperazine-1-carboxylate;

2-methylpropyl 4-{3-cyclobutyl-1-(4-fluorophenyl)-6-[(morpholine-4-sulfonyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperazine-1-carboxylate;

2-methylpropyl 4-{3-cyclobutyl-1-(4-fluorophenyl)-6-[(2-methoxyethanesulfonyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperazine-1-carboxylate;

2-methylpropyl 4-{3-cyclobutyl-1-(4-fluorophenyl)-6-[(methylsulfamoyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperazine-1-carboxylate;

3-cyclobutyl-1-(4-fluorophenyl)-4-(9-methyl-3,9-diazaspiro[5.5]undecan-3-yl)-*N*-(morpholine-4-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide; and

N-(2-aminopyridine-3-sulfonyl)-3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide.

[00246] Compounds of the invention are named by using Name 2015 naming algorithm by Advanced Chemical Development, Struct=Name naming algorithm as part of CHEMDRAW® ULTRA v. 12.0.2.1076, or Accelrys Draw 4.2.

[00247] Compounds of the invention may exist as stereoisomers wherein asymmetric or chiral centers are present. These stereoisomers are "*R*" or "*S*" depending on the configuration of substituents around the chiral carbon atom. The terms "*R*" and "*S*" used herein are configurations as defined in IUPAC 1974 Recommendations for Section E, Fundamental Stereochemistry, in Pure Appl. Chem., 1976, 45: 13-30. The invention contemplates various stereoisomers and mixtures thereof and these are specifically included within the scope of this invention. Stereoisomers include enantiomers and diastereomers, and mixtures of enantiomers or diastereomers. Individual stereoisomers of compounds of the invention may be prepared synthetically from commercially available starting materials which contain asymmetric or chiral

centers or by preparation of racemic mixtures followed by methods of resolution well-known to those of ordinary skill in the art. These methods of resolution are exemplified by (1) attachment of a mixture of enantiomers to a chiral auxiliary, separation of the resulting mixture of diastereomers by recrystallization or chromatography and optional liberation of the optically pure product from the auxiliary as described in Furniss, Hannaford, Smith, and Tatchell, "Vogel's Textbook of Practical Organic Chemistry", 5th edition (1989), Longman Scientific & Technical, Essex CM20 2JE, England, or (2) direct separation of the mixture of optical enantiomers on chiral chromatographic columns or (3) fractional recrystallization methods.

[00248] Compounds of the invention may exist as *cis* or *trans* isomers, wherein substituents on a ring may attached in such a manner that they are on the same side of the ring (*cis*) relative to each other, or on opposite sides of the ring relative to each other (*trans*). For example, cyclobutane may be present in the *cis* or *trans* configuration, and may be present as a single isomer or a mixture of the *cis* and *trans* isomers. Individual *cis* or *trans* isomers of compounds of the invention may be prepared synthetically from commercially available starting materials using selective organic transformations, or prepared in single isomeric form by purification of mixtures of the *cis* and *trans* isomers. Such methods are well-known to those of ordinary skill in the art, and may include separation of isomers by recrystallization or chromatography.

[00249] It should be understood that the compounds of the invention may possess tautomeric forms, as well as geometric isomers, and that these also constitute an aspect of the invention.

[00250] The present disclosure includes all pharmaceutically acceptable isotopically-labelled compounds of formula (I) wherein one or more atoms are replaced by atoms having the same atomic number, but an atomic mass or mass number different from the atomic mass or mass number which predominates in nature. Examples of isotopes suitable for inclusion in the compounds of the disclosure include isotopes of hydrogen, such as ^{2}H and ^{3}H, carbon, such as ^{11}C, ^{13}C and ^{14}C, chlorine, such as ^{36}Cl, fluorine, such as ^{18}F, iodine, such as ^{123}I and ^{125}I, nitrogen, such as ^{13}N and ^{15}N, oxygen, such as ^{15}O, ^{17}O and ^{18}O, phosphorus, such as ^{32}P, and sulphur, such as ^{35}S. Certain isotopically-labelled compounds of formula (I), for example, those incorporating a radioactive isotope, are useful in drug and/or substrate tissue distribution studies. The radioactive isotopes tritium, *i.e.* ^{3}H, and carbon-14, *i.e.* ^{14}C, are particularly useful for this purpose in view of their ease of incorporation and ready means of detection. Substitution with heavier isotopes such as deuterium, *i.e.* ^{2}H, may afford certain therapeutic advantages resulting

from greater metabolic stability, for example, increased *in vivo* half-life or reduced dosage requirements, and hence may be preferred in some circumstances. Substitution with positron emitting isotopes, such as ^{11}C, ^{18}F, ^{15}O and ^{13}N, can be useful in Positron Emission Topography (PET) studies for examining substrate receptor occupancy. Isotopically-labeled compounds of formula (I) may generally be prepared by conventional techniques known to those skilled in the art or by processes analogous to those described in the accompanying Examples using an appropriate isotopically-labeled reagents in place of the non-labeled reagent previously employed.

[00251] Thus, the formula drawings within this specification can represent only one of the possible tautomeric, geometric, or stereoisomeric forms. It is to be understood that the invention encompasses any tautomeric, geometric, or stereoisomeric form, and mixtures thereof, and is not to be limited merely to any one tautomeric, geometric, or stereoisomeric form utilized within the formula drawings.

[00252] Compounds of formula (I) may be used in the form of pharmaceutically acceptable salts. The phrase "pharmaceutically acceptable salt" means those salts which are, within the scope of sound medical judgement, suitable for use in contact with the tissues of humans and lower animals without undue toxicity, irritation, allergic response and the like and are commensurate with a reasonable benefit/risk ratio.

[00253] Pharmaceutically acceptable salts have been described in S. M. Berge et al. J. Pharmaceutical Sciences, 1977, 66: 1-19.

[00254] Compounds of formula (I) may contain either a basic or an acidic functionality, or both, and can be converted to a pharmaceutically acceptable salt, when desired, by using a suitable acid or base. The salts may be prepared in situ during the final isolation and purification of the compounds of the invention.

[00255] Examples of acid addition salts include, but are not limited to acetate, adipate, alginate, citrate, aspartate, benzoate, benzenesulfonate, bisulfate, butyrate, camphorate, camphorsulfonate, digluconate, glycerophosphate, hemisulfate, heptanoate, hexanoate, fumarate, hydrochloride, hydrobromide, hydroiodide, 2-hydroxyethansulfonate (isothionate), lactate, malate, maleate, methanesulfonate, nicotinate, 2-naphthalenesulfonate, oxalate, palmitoate, pectinate, persulfate, 3-phenylpropionate, picrate, pivalate, propionate, succinate, tartrate, thiocyanate, phosphate, glutamate, bicarbonate, p-toluenesulfonate and undecanoate. Also, the

basic nitrogen-containing groups may be quaternized with such agents as lower alkyl halides such as, but not limited to, methyl, ethyl, propyl, and butyl chlorides, bromides and iodides; dialkyl sulfates like dimethyl, diethyl, dibutyl and diamyl sulfates; long chain halides such as, but not limited to, decyl, lauryl, myristyl and stearyl chlorides, bromides and iodides; arylalkyl halides like benzyl and phenethyl bromides and others. Water or oil-soluble or dispersible products are thereby obtained. Examples of acids which may be employed to form pharmaceutically acceptable acid addition salts include such inorganic acids as hydrochloric acid, hydrobromic acid, sulfuric acid, and phosphoric acid and such organic acids as acetic acid, fumaric acid, maleic acid, 4-methylbenzenesulfonic acid, succinic acid, and citric acid.

[00256] Basic addition salts may be prepared in situ during the final isolation and purification of compounds of this invention by reacting a carboxylic acid-containing moiety with a suitable base such as, but not limited to, the hydroxide, carbonate or bicarbonate of a pharmaceutically acceptable metal cation or with ammonia or an organic primary, secondary or tertiary amine. Pharmaceutically acceptable salts include, but are not limited to, cations based on alkali metals or alkaline earth metals such as, but not limited to, lithium, sodium, potassium, calcium, magnesium and aluminum salts and the like and nontoxic quaternary ammonia and amine cations including ammonium, tetramethylammonium, tetraethylammonium, methylamine, dimethylamine, trimethylamine, triethylamine, diethylamine, ethylamine and the like. Other examples of organic amines useful for the formation of base addition salts include ethylenediamine, ethanolamine, diethanolamine, piperidine, piperazine and the like.

[00257] The term "pharmaceutically acceptable prodrug" or "prodrug" as used herein refers to derivatives of the compounds of the invention which have cleavable groups. Such derivatives become, by solvolysis or under physiological conditions, the compounds of the invention which are pharmaceutically active *in vivo*. Prodrugs of the compounds of the invention are, within the scope of sound medical judgement, suitable for use in contact with the tissues of humans and lower animals without undue toxicity, irritation, allergic response, and the like, commensurate with a reasonable benefit/risk ratio, and effective for their intended use.

[00258] The invention contemplates compounds of formula (I) formed by synthetic means or formed by in vivo biotransformation of a prodrug.

[00259] Compounds described herein may exist in unsolvated as well as solvated forms, including hydrated forms, such as hemi-hydrates. In general, the solvated forms, with

pharmaceutically acceptable solvents such as water and ethanol among others are equivalent to the unsolvated forms for the purposes of the invention.

Pharmaceutical Compositions

[00260] When employed as a pharmaceutical, a compound of the invention is typically administered in the form of a pharmaceutical composition. Such compositions can be prepared in a manner well known in the pharmaceutical art and comprise a therapeutically effective amount of a compound of formula (I), or a pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable carrier. The phrase "pharmaceutical composition" refers to a composition suitable for administration in medical or veterinary use.

[00261] The pharmaceutical compositions that comprise a compound of formula (I), alone or in combination with further therapeutically active ingredient, may be administered to the subjects orally, rectally, parenterally, intracisternally, intravaginally, intraperitoneally, topically (as by powders, ointments or drops), bucally or as an oral or nasal spray. The term "parenterally" as used herein, refers to modes of administration which include intravenous, intramuscular, intraperitoneal, intrasternal, subcutaneous and intraarticular injection and infusion.

[00262] The term "pharmaceutically acceptable carrier" as used herein, means a non-toxic, inert solid, semi-solid or liquid filler, diluent, encapsulating material or formulation auxiliary of any type. Some examples of materials which may serve as pharmaceutically acceptable carriers are sugars such as, but not limited to, lactose, glucose and sucrose; starches such as, but not limited to, corn starch and potato starch; cellulose and its derivatives such as, but not limited to, sodium carboxymethyl cellulose, ethyl cellulose and cellulose acetate; powdered tragacanth; malt; gelatin; talc; excipients such as, but not limited to, cocoa butter and suppository waxes; oils such as, but not limited to, peanut oil, cottonseed oil, safflower oil, sesame oil, olive oil, corn oil and soybean oil; glycols; such a propylene glycol; esters such as, but not limited to, ethyl oleate and ethyl laurate; agar; buffering agents such as, but not limited to, magnesium hydroxide and aluminum hydroxide; alginic acid; pyrogen-free water; isotonic saline; Ringer's solution; ethyl alcohol, and phosphate buffer solutions, as well as other non-toxic compatible lubricants such as, but not limited to, sodium lauryl sulfate and magnesium stearate, as well as coloring agents, releasing agents, coating agents, sweetening, flavoring and perfuming agents, preservatives and

antioxidants may also be present in the composition, according to the judgment of the formulator.

[00263] Pharmaceutical compositions for parenteral injection comprise pharmaceutically acceptable sterile aqueous or nonaqueous solutions, dispersions, suspensions or emulsions as well as sterile powders for reconstitution into sterile injectable solutions or dispersions just prior to use. Examples of suitable aqueous and nonaqueous diluents, solvents, or vehicles include water, ethanol, polyols (such as glycerol, propylene glycol, polyethylene glycol and the like), vegetable oils (such as olive oil), injectable organic esters (such as ethyl oleate), and suitable mixtures thereof. Proper fluidity may be maintained, for example, by the use of coating materials such as lecithin, by the maintenance of the required particle size in the case of dispersions and by the use of surfactants.

[00264] These compositions may also contain adjuvants such as preservatives, wetting agents, emulsifying agents and dispersing agents. Prevention of the action of microorganisms may be ensured by the inclusion of various antibacterial and antifungal agents, for example, paraben, chlorobutanol, phenol sorbic acid, and the like. It may also be desirable to include isotonic agents such as sugars, sodium chloride, and the like. Prolonged absorption of the injectable pharmaceutical form may be brought about by the inclusion of agents which delay absorption, such as aluminum monostearate and gelatin.

[00265] In some cases, in order to prolong the effect of the drug, it may be desirable to slow the absorption of the drug from subcutaneous or intramuscular injection. This may be accomplished by the use of a liquid suspension of crystalline or amorphous material with poor water solubility. The rate of absorption of the drug then depends upon its rate of dissolution which, in turn, may depend upon crystal size and crystalline form. Alternatively, delayed absorption of a parenterally-administered drug form may be accomplished by dissolving or suspending the drug in an oil vehicle.

[00266] Injectable depot forms are made by forming microencapsule matrices of the drug in biodegradable polymers such as polylactide-polyglycolide. Depending upon the ratio of drug to polymer and the nature of the particular polymer employed, the rate of drug release may be controlled. Examples of other biodegradable polymers include poly(orthoesters) and poly(anhydrides). Depot injectable formulations are also prepared by entrapping the drug in liposomes or microemulsions which are compatible with body tissues.

[00267] The injectable formulations may be sterilized, for example, by filtration through a bacterial-retaining filter or by incorporating sterilizing agents in the form of sterile solid compositions which can be dissolved or dispersed in sterile water or other sterile injectable medium just prior to use.

[00268] Solid dosage forms for oral administration include capsules, tablets, pills, powders, and granules. In certain embodiments, solid dosage forms may contain from 1% to 95% (w/w) of a compound of formula (I). In certain embodiments, the compound of formula (I), or pharmaceutically acceptable salts thereof, may be present in the solid dosage form in a range of from 5% to 70% (w/w). In such solid dosage forms, the active compound may be mixed with at least one inert, pharmaceutically acceptable carrier, such as sodium citrate or dicalcium phosphate and/or a), fillers or extenders such as starches, lactose, sucrose, glucose, mannitol, and silicic acid; b) binders such as carboxymethylcellulose, alginates, gelatin, polyvinylpyrrolidone, sucrose, and acacia; c) humectants such as glycerol; d) disintegrating agents such as agar-agar, calcium carbonate, potato or tapioca starch, alginic acid, certain silicates, and sodium carbonate; e) solution retarding agents such as paraffin; f) absorption accelerators such as quaternary ammonium compounds; g) wetting agents such as cetyl alcohol and glycerol monostearate; h) absorbents such as kaolin and bentonite clay and i) lubricants such as talc, calcium stearate, magnesium stearate, solid polyethylene glycols, sodium lauryl sulfate and mixtures thereof. In the case of capsules, tablets and pills, the dosage form may also comprise buffering agents.

[00269] The pharmaceutical composition may be a unit dosage form. In such form the preparation is subdivided into unit doses containing appropriate quantities of the active component. The unit dosage form can be a packaged preparation, the package containing discrete quantities of preparation, such as packeted tablets, capsules, and powders in vials or ampules. Also, the unit dosage form may be a capsule, tablet, cachet, or lozenge itself, or it may be the appropriate number of any of these in packaged form. The quantity of active component in a unit dose preparation may be varied or adjusted from 0.1 mg to 1000 mg, from 1 mg to 100 mg, or from 1% to 95% (w/w) of a unit dose, according to the particular application and the potency of the active component. The composition may, if desired, also contain other compatible therapeutic agents.

[00270] The dose to be administered to a subject may be determined by the efficacy of the particular compound employed and the condition of the subject, as well as the body weight or

surface area of the subject to be treated. The size of the dose also will be determined by the existence, nature, and extent of any adverse side-effects that accompany the administration of a particular compound in a particular subject. In determining the effective amount of the compound to be administered in the treatment or prophylaxis of the disorder being treated, the physician may evaluate factors such as the circulating plasma levels of the compound, compound toxicities, and/or the progression of the disease, etc.

[00271] For administration, compounds may be administered at a rate determined by factors that may include, but are not limited to, the LD_{50} of the compound, the pharmacokinetic profile of the compound, contraindicated drugs, and the side-effects of the compound at various concentrations, as applied to the mass and overall health of the subject. Administration may be accomplished via single or divided doses.

[00272] The compounds utilized in the pharmaceutical method of the invention may be administered at the initial dosage of about 0.001 mg/kg to about 100 mg/kg daily. In certain embodiments, the daily dose range is from about 0.1 mg/kg to about 10 mg/kg. The dosages, however, may be varied depending upon the requirements of the subject, the severity of the condition being treated, and the compound being employed. Determination of the proper dosage for a particular situation is within the skill of the practitioner. Treatment may be initiated with smaller dosages, which are less than the optimum dose of the compound. Thereafter, the dosage is increased by small increments until the optimum effect under circumstances is reached. For convenience, the total daily dosage may be divided and administered in portions during the day, if desired.

[00273] Solid compositions of a similar type may also be employed as fillers in soft and hard-filled gelatin capsules using such carriers as lactose or milk sugar as well as high molecular weight polyethylene glycols and the like.

[00274] The solid dosage forms of tablets, dragees, capsules, pills and granules can be prepared with coatings and shells such as enteric coatings and other coatings well-known in the pharmaceutical formulating art. They may optionally contain opacifying agents and may also be of a composition such that they release the active ingredient(s) only, or preferentially, in a certain part of the intestinal tract, optionally, in a delayed manner. Examples of embedding compositions which can be used include polymeric substances and waxes.

[00275] The active compounds may also be in micro-encapsulated form, if appropriate, with one or more of the above-mentioned carriers.

[00276] Liquid dosage forms for oral administration include pharmaceutically acceptable emulsions, solutions, suspensions, syrups and elixirs. In addition to the active compounds, the liquid dosage forms may contain inert diluents commonly used in the art such as, for example, water or other solvents, solubilizing agents and emulsifiers such as ethyl alcohol, isopropyl alcohol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propylene glycol, 1,3-butylene glycol, dimethyl formamide, oils (in particular, cottonseed, groundnut, corn, germ, olive, castor and sesame oils), glycerol, tetrahydrofurfuryl alcohol, polyethylene glycols, and fatty acid esters of sorbitan and mixtures thereof.

[00277] Besides inert diluents, the oral compositions may also include adjuvants such as wetting agents, emulsifying and suspending agents, sweetening, flavoring and perfuming agents. Suspensions, in addition to the active compounds, may contain suspending agents as, for example, ethoxylated isostearyl alcohols, polyoxyethylene sorbitol and sorbitan esters, microcrystalline cellulose, aluminum metahydroxide, bentonite, agar-agar, tragacanth and mixtures thereof.

[00278] Compositions for rectal or vaginal administration are preferably suppositories which may be prepared by mixing the compounds with suitable non-irritating carriers or carriers such as cocoa butter, polyethylene glycol, or a suppository wax which are solid at room temperature but liquid at body temperature and therefore melt in the rectum or vaginal cavity and release the active compound.

[00279] Compounds may also be administered in the form of liposomes. Liposomes generally may be derived from phospholipids or other lipid substances. Liposomes are formed by mono- or multi-lamellar hydrated liquid crystals which are dispersed in an aqueous medium. Any non-toxic, physiologically acceptable and metabolizable lipid capable of forming liposomes may be used. The present compositions in liposome form may contain, in addition to a compound of the invention, stabilizers, preservatives, excipients, and the like. Examples of lipids include, but are not limited to, natural and synthetic phospholipids, and phosphatidyl cholines (lecithins), used separately or together.

[00280] Methods to form liposomes have been described, see example, Prescott, Ed., Methods in Cell Biology, Volume XIV, Academic Press, New York, N.Y. (l976), p. 33 et seq.

Dosage forms for topical administration of a compound described herein include powders, sprays, ointments, and inhalants. The active compound may be mixed under sterile conditions with a pharmaceutically acceptable carrier and any needed preservatives, buffers or propellants which may be required. Opthalmic formulations, eye ointments, powders and solutions are also contemplated as being within the scope of this invention.

[00281] A compound of the invention may also be administered in sustained release forms or from sustained release drug delivery systems.

Methods of Use

[00282] The compounds and compositions using any amount and any route of administration may be administered to a subject for the treatment or prevention of cystic fibrosis, pancreatic insufficiency, Sjögren's Syndrome (SS), chronic obstructive lung disease (COLD), or chronic obstructive airway disease (COAD).

[00283] The term "administering" refers to the method of contacting a compound with a subject. Thus, the compounds may be administered by injection, that is, intravenously, intramuscularly, intracutaneously, subcutaneously, intraduodenally, parentally, or intraperitoneally. Also, the compounds described herein may be administered by inhalation, for example, intranasally. Additionally, the compounds may be administered transdermally, topically, and via implantation. In certain embodiments, the compounds and compositions thereof may be delivered orally. The compounds may also be delivered rectally, bucally, intravaginally, ocularly, or by insufflation. CFTR-modulated disorders and conditions may be treated prophylactically, acutely, and chronically using compounds and compositions thereof, depending on the nature of the disorder or condition. Typically, the host or subject in each of these methods is human, although other mammals may also benefit from the administration of compounds and compositions thereof as set forth hereinabove.

[00284] Compounds of the invention are useful as modulators of CFTR. Thus, the compounds and compositions are particularly useful for treating or lessening the severity or progression of a disease, disorder, or a condition where hyperactivity or inactivity of CFTR is involved. Accordingly, the invention provides a method for treating cystic fibrosis, pancreatic insufficiency, Sjögren's Syndrome (SS), chronic obstructive lung disease (COLD), or chronic obstructive airway disease (COAD) in a subject, wherein the method comprises the step of

administering to said subject a therapeutically effective amount of a compound of formula (I), or a pharmaceutically acceptable salt thereof, or a preferred embodiment thereof as set forth above, with or without a pharmaceutically acceptable carrier. Particularly, the method is for the treatment or prevention of cystic fibrosis. In a more particular embodiment, the cystic fibrosis is caused by a Class I, II, III, IV, V, and/or VI mutation.

[00285] One embodiment is directed to a compound of the invention or a pharmaceutically acceptable salt thereof, or pharmaceutical compositions comprising a compound of the invention for use in medicine. One embodiment is directed to a compound of the invention or a pharmaceutically acceptable salt thereof, or pharmaceutical compositions thereof, for use in the treatment of cystic fibrosis, pancreatic insufficiency, Sjögren's Syndrome (SS), chronic obstructive lung disease (COLD) or chronic obstructive airway disease (COAD). In a more particular embodiment, the present invention provides compounds of the invention or pharmaceutically acceptable salts thereof, or pharmaceutical compositions comprising thereof, for use in the treatment of cystic fibrosis. In a more particular embodiment, the cystic fibrosis is caused by a Class I, II, III, IV, V, and/or VI mutation.

[00286] One embodiment is directed to the use of a compound according to formula (I) or a pharmaceutically acceptable salt thereof in the preparation of a medicament. The medicament optionally can comprise one or more additional therapeutic agents. In some embodiments, the medicament is for use in the treatment of cystic fibrosis, pancreatic insufficiency, Sjögren's Syndrome (SS), chronic obstructive lung disease (COLD) or chronic obstructive airway disease (COAD). In a particular embodiment, the medicament is for use in the treatment of cystic fibrosis. In a more particular embodiment, the cystic fibrosis is caused by a Class I, II, III, IV, V, and/or VI mutation.

[00287] This invention also is directed to the use of a compound according to formula (I) or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of cystic fibrosis, Sjögren's syndrome, pancreatic insufficiency, chronic obstructive lung disease, and chronic obstructive airway disease. The medicament optionally can comprise one or more additional therapeutic agents. In a particular embodiment, the invention is directed to the use of a compound according to formula (I) or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of cystic fibrosis. In a more particular embodiment, the cystic fibrosis is caused by a Class I, II, III, IV, V, and/or VI mutation.

[00288] In one embodiment, the present invention provides pharmaceutical compositions comprising a compound of the invention or a pharmaceutically acceptable salt thereof, and one or more additional therapeutic agents. In a particular embodiment, the other therapeutic agent is a cystic fibrosis treatment agent. In a more particular embodiment, the cystic fibrosis is caused by a Class I, II, III, IV, V, and/or VI mutation.

[00289] The present compounds or pharmaceutically acceptable salts thereof may be administered as the sole active agent or it may be co-administered with other therapeutic agents, including other compounds or pharmaceutically acceptable salts thereof that demonstrate the same or a similar therapeutic activity and that are determined to be safe and efficacious for such combined administration. The present compounds may be co-administered to a subject. The term "co-administered" means the administration of two or more different therapeutic agents to a subject in a single pharmaceutical composition or in separate pharmaceutical compositions. Thus co-administration involves administration at the same time of a single pharmaceutical composition comprising two or more therapeutic agents or administration of two or more different compositions to the same subject at the same or different times.

[00290] The compounds of the invention or a pharmaceutically acceptable salt thereof may be co-administered with a therapeutically effective amount of one or more additional therapeutic agents to treat a CFTR mediated disease, where examples of the therapeutic agents include, but are not limited to antibiotics (for example, aminoglycosides, colistin, aztreonam, ciprofloxacin, and azithromycin), expectorants (for example, hypertonic saline, acetylcysteine, dornase alfa, and denufosol), pancreatic enzyme supplements (for example, pancreatin, and pancrelipase), epithelial sodium channel blocker (ENaC) inhibitors, CFTR modulators (for example, CFTR potentiators, CFTR correctors), and CFTR amplifiers. In one embodiment, the CFTR mediated disease is cystic fibrosis, chronic obstructive pulmonary disease (COPD), dry eye disease, pancreatic insufficiency, or Sjogren's syndrome. In one embodiment, the CFTR mediated disease is cystic fibrosis. In one embodiment, the compounds of the invention or pharmaceutically acceptable salts thereof may be co-administered with one or two CFTR modulators and one CFTR amplifier. In one embodiment, the compounds of the invention or pharmaceutically acceptable salts thereof may be co-administered with one potentiator, one or more correctors, and one CFTR amplifier. In one embodiment, the compounds of the invention or pharmaceutically acceptable salts thereof may be co-administered with one or more CFTR

modulators. In one embodiment, the compounds of the invention or pharmaceutically acceptable salts thereof may be co-administered with one CFTR modulators. In one embodiment, the compounds of the invention or pharmaceutically acceptable salts thereof may be co-administered with two CFTR modulators. In one embodiment, the compounds of the invention or pharmaceutically acceptable salts thereof may be co-administered with three CFTR modulators. In one embodiment, the compounds of the invention or pharmaceutically acceptable salts thereof may be co-administered with one potentiator and one or more correctors. In one embodiment, the compounds of the invention or pharmaceutically acceptable salts thereof may be co-administered with one potentiator and one corrector. In one embodiment, the compounds of the invention or pharmaceutically acceptable salts thereof may be co-administered with one potentiator and two correctors. In one embodiment, the compounds of the invention or pharmaceutically acceptable salts thereof may be co-administered with one potentiator. In one embodiment, the compounds of the invention or pharmaceutically acceptable salts thereof may be co-administered with one or more correctors. In one embodiment, the compounds of the invention or pharmaceutically acceptable salts thereof may be co-administered with one corrector. In one embodiment, the compounds of the invention or pharmaceutically acceptable salts thereof may be co-administered with two correctors.

[00291] Examples of CFTR potentiators include, but are not limited to, Ivacaftor (VX-770), CTP-656, NVS-QBW251, FD1860293, PTI-808, GLPG2451, GLPG1837, *N*-(3-carbamoyl-5,5,7,7-tetramethyl-5,7-dihydro-4*H*-thieno[2,3-*c*]pyran-2-yl)-1*H*-pyrazole-5-carboxamide and 3-amino-*N*-[(2*S*)-2-hydroxypropyl]-5-{[4-(trifluoromethoxy)phenyl]sulfonyl}pyridine-2-carboxamide. Examples of potentiators are also disclosed in publications: WO2005120497, WO2008147952, WO2009076593, WO2010048573, WO2006002421, WO2011072241, WO2011113894, WO2013038373, WO2013038378, WO2013038381, WO2013038386, WO2013038390, WO2014180562, WO2015018823; and US Applications 14/271,080, 14/451,619, and 15/164,317.

[00292] In one embodiment, the potentiator can be selected from the group consisting of:

Ivacaftor (VX-770, *N*-(2,4-di-*tert*-butyl-5-hydroxyphenyl)-4-oxo-1,4-dihydroquinoline-3-carboxamide);

CTP-656;

NVS-QBW251;

FD1860293;

PTI-808;

GLPG1837;

GLPG2451;

2-(2-fluorobenzamido)-5,5,7,7-tetramethyl-5,7-dihydro-4*H*-thieno[2,3-*c*]pyran-3-carboxamide;

N-(3-carbamoyl-5,5,7,7-tetramethyl-4,7-dihydro-5*H*-thieno[2,3-*c*]pyran-2-yl)-1*H*-pyrazole-5-carboxamide;

2-(2-hydroxybenzamido)-5,5,7,7-tetramethyl-5,7-dihydro-4*H*-thieno[2,3-*c*]pyran-3-carboxamide;

2-(1-hydroxycyclopropanecarboxamido)-5,5,7,7-tetramethyl-5,7-dihydro-4*H*-thieno[2,3-*c*]pyran-3-carboxamide;

5,5,7,7-tetramethyl-2-(2-(trifluoromethyl)benzamido)-5,7-dihydro-4*H*-thieno[2,3-*c*]pyran-3-carboxamide;

2-(2-hydroxy-2-methylpropanamido)-5,5,7,7-tetramethyl-5,7-dihydro-4*H*-thieno[2,3-*c*]pyran-3-carboxamide;

2-(1-(hydroxymethyl)cyclopropanecarboxamido)-5,5,7,7-tetramethyl-5,7-dihydro-4*H*-thieno[2,3-*c*]pyran-3-carboxamide;

2-(3-hydroxy-2,2-dimethylpropanamido)-5,5,7,7-tetramethyl-5,7-dihydro-4*H*-thieno[2,3-*c*]pyran-3-carboxamide;

N-(3-carbamoyl-5,5,7,7-tetramethyl-5,7-dihydro-4*H*-thieno[2,3-*c*]pyran-2-yl)-5-methyl-1*H*-pyrazole-3-carboxamide;

N-(3-carbamoyl-5,5,7,7-tetramethyl-5,7-dihydro-4*H*-thieno[2,3-*c*]pyran-2-yl)-5-cyclopropyl-1*H*-pyrazole-3-carboxamide;

N-(3-carbamoyl-5,5,7,7-tetramethyl-5,7-dihydro-4*H*-thieno[2,3-*c*]pyran-2-yl)-5-isopropyl-1*H*-pyrazole-3-carboxamide;

N-(3-carbamoyl-5,5,7,7-tetramethyl-5,7-dihydro-4*H*-thieno[2,3-*c*]pyran-2-yl)-5-(trifluoromethyl)-1*H*-pyrazole-3-carboxamide;

5-*tert*-butyl-*N*-(3-carbamoyl-5,5,7,7-tetramethyl-5,7-dihydro-4*H*-thieno[2,3-*c*]pyran-2-yl)-1*H*-pyrazole-3-carboxamide;

N-(3-carbamoyl-5,5,7,7-tetramethyl-5,7-dihydro-4*H*-thieno[2,3-*c*]pyran-2-yl)-5-ethyl-1*H*-pyrazole-3-carboxamide;

N-(3-carbamoyl-5,5,7,7-tetramethyl-5,7-dihydro-4*H*-thieno[2,3-*c*]pyran-2-yl)-3-ethyl-4-methyl-1*H*-pyrazole-5-carboxamide;

2-(2-hydroxypropanamido)-5,5,7,7-tetramethyl-5,7-dihydro-4*H*-thieno[2,3-*c*]pyran-3-carboxamide;

N-(3-carbamoyl-5,5,7,7-tetramethyl-5,7-dihydro-4*H*-thieno[2,3-*c*]pyran-2-yl)-4-chloro-1*H*-pyrazole-3-carboxamide;

N-(3-carbamoyl-5,5,7,7-tetramethyl-5,7-dihydro-4*H*-thieno[2,3-*c*]pyran-2-yl)-1,4,6,7-tetrahydropyrano[4,3-*c*]pyrazole-3-carboxamide;

4-bromo-*N*-(3-carbamoyl-5,5,7,7-tetramethyl-5,7-dihydro-4*H*-thieno[2,3-*c*]pyran-2-yl)-1*H*-pyrazole-3-carboxamide;

N-(3-carbamoyl-5,5,7,7-tetramethyl-5,7-dihydro-4*H*-thieno[2,3-*c*]pyran-2-yl)-4-chloro-5-methyl-1*H*-pyrazole-3-carboxamide;

N-(3-carbamoyl-5,5,7,7-tetramethyl-5,7-dihydro-4*H*-thieno[2,3-*c*]pyran-2-yl)-4-methyl-1*H*-pyrazole-3-carboxamide;

2-(2-hydroxy-3,3-dimethylbutanamido)-5,5,7,7-tetramethyl-5,7-dihydro-4*H*-thieno[2,3-*c*]pyran-3-carboxamide;

2-[(2-hydroxy-4-methyl-pentanoyl)amino]-5,5,7,7-tetramethyl-4*H*-thieno[2,3-*c*]pyran-3-carboxamide;

5-(2-methoxy-ethoxy)-1*H*-pyrazole-3-carboxylic acid (3-carbamoyl-5,5,7,7-tetramethyl-4,7-dihydro-5*H*-thieno[2,3-*c*]pyran-2-yl)-amide;

N-(3-carbamoyl-5,5,7,7-tetramethyl-4*H*-thieno[2,3-*c*]pyran-2-yl)-4-(3-methoxypropyl)-1*H*-pyrazole-3-carboxamide;

N-(3-carbamoyl-5,5,7,7-tetramethyl-4*H*-thieno[2,3-*c*]pyran-2-yl)-4-(2-ethoxyethyl)-1*H*-pyrazole-3-carboxamide;

2-[[(2*S*)-2-hydroxy-3,3-dimethyl-butanoyl]amino]-5,5,7,7-tetramethyl-4*H*-thieno[2,3-*c*]pyran-3-carboxamide;

2-[[(2*R*)-2-hydroxy-3,3-dimethyl-butanoyl]amino]-5,5,7,7-tetramethyl-4*H*-thieno[2,3-*c*]pyran-3-carboxamide;

2-[(2-hydroxy-2,3,3-trimethyl-butanoyl)amino]-5,5,7,7-tetramethyl-4*H*-thieno[2,3-*c*]pyran-3-carboxamide;

[5-[(3-carbamoyl-5,5,7,7-tetramethyl-4*H*-thieno[2,3-*c*]pyran-2-yl)carbamoyl]pyrazol-1-yl]methyl dihydrogen phosphate;

[3-[(3-carbamoyl-5,5,7,7-tetramethyl-4*H*-thieno[2,3-*c*]pyran-2-yl)carbamoyl]pyrazol-1-yl]methyl dihydrogen phosphate;

N-(3-carbamoyl-5,5,7,7-tetramethyl-4*H*-thieno[2,3-*c*]pyran-2-yl)-4-(1,4-dioxan-2-yl)-1*H*-pyrazole-3-carboxamide;

5,5,7,7-tetramethyl-2-[[(2*S*)-3,3,3-trifluoro-2-hydroxy-2-methyl-propanoyl]amino]-4*H*-thieno[2,3-*c*]pyran-3-carboxamide;

2-[[(2*S*)-2-hydroxypropanoyl]amino]-5,5,7,7-tetramethyl-4*H*-thieno[2,3-*c*]pyran-3-carboxamide;

3-amino-*N*-(2-hydroxy-2-methylpropyl)-5-{[4-(trifluoromethoxy)phenyl]sulfonyl}pyridine-2-carboxamide;

3-amino-*N*-[(4-hydroxy-1-methylpiperidin-4-yl)methyl]-5-{[4-(trifluoromethoxy)phenyl]sulfonyl}pyridine-2-carboxamide;

3-amino-*N*-(3-hydroxy-2,2-dimethylpropyl)-5-{[4-(trifluoromethoxy)phenyl]sulfonyl}pyridine-2-carboxamide;

3-amino-5-[(4-fluorophenyl)sulfonyl]-*N*-[(1-hydroxycyclopropyl)methyl]pyridine-2-carboxamide;

3-amino-5-[(4-fluorophenyl)sulfonyl]-*N*-[(2*R*)-3,3,3-trifluoro-2-hydroxypropyl]pyridine-2-carboxamide;

3-amino-5-[(3-fluorophenyl)sulfonyl]-*N*-(2-hydroxy-2-methylpropyl)pyridine-2-carboxamide;

3-amino-*N*-[2-(cyclopropylamino)-2-oxoethyl]-5-{[4-(trifluoromethoxy)phenyl]sulfonyl}pyridine-2-carboxamide;

(3-amino-5-{[4-(trifluoromethoxy)phenyl]sulfonyl}pyridin-2-yl)(azetidin-1-yl)methanone;

(3-amino-5-{[4-(trifluoromethoxy)phenyl]sulfonyl}pyridin-2-yl)[3-(hydroxymethyl)azetidin-1-yl]methanone;

(3-amino-5-{[4-(trifluoromethoxy)phenyl]sulfonyl}pyridin-2-yl)(3-fluoroazetidin-1-yl)methanone;

3-amino-*N*-[(2*R*)-2-hydroxy-3-methoxypropyl]-5-{[4-(trifluoromethyl)phenyl]sulfonyl}pyridine-2-carboxamide;

(3-amino-5-{[2-fluoro-4-(trifluoromethoxy)phenyl]sulfonyl}pyridin-2-yl)(3-hydroxyazetidin-1-yl)methanone;

(3-amino-5-{[2-(trifluoromethoxy)phenyl]sulfonyl}pyridin-2-yl)(3,3-difluoroazetidin-1-yl)methanone;

rac-3-amino-*N*-[(3*R*,4*S*)-4-hydroxytetrahydro-2*H*-pyran-3-yl]-5-{[2-(trifluoromethoxy)phenyl]sulfonyl}pyridine-2-carboxamide;

3-amino-5-[(4,4-difluoropiperidin-1-yl)sulfonyl]-*N*-(3,3,3-trifluoro-2-hydroxypropyl)pyridine-2-carboxamide;

(3-amino-5-{[2-(trifluoromethoxy)phenyl]sulfonyl}pyridin-2-yl)[3-hydroxy-3-(trifluoromethyl)azetidin-1-yl]methanone;

3-amino-*N*-(2-hydroxy-4-methylpentyl)-5-{[4-(trifluoromethoxy)phenyl]sulfonyl}pyridine-2-carboxamide;

(3-amino-5-{[4-(trifluoromethyl)phenyl]sulfonyl}pyridin-2-yl)(3-hydroxy-3-methylazetidin-1-yl)methanone;

3-amino-*N*-(3,3,3-trifluoro-2-hydroxypropyl)-5-{[4-(trifluoromethyl)piperidin-1-yl]sulfonyl}pyridine-2-carboxamide;

3-amino-*N*-[2-hydroxy-1-(4-methoxyphenyl)ethyl]-5-{[4-(trifluoromethoxy)phenyl]sulfonyl}pyridine-2-carboxamide;

3-amino-5-[(3,3-difluoroazetidin-1-yl)sulfonyl]-*N*-(3,3,3-trifluoro-2-hydroxypropyl)pyridine-2-carboxamide;

3-amino-5-{[2-fluoro-4-(trifluoromethyl)phenyl]sulfonyl}-*N*-[(2*S*)-2-hydroxypropyl]pyridine-2-carboxamide;

3-amino-5-{[2-fluoro-4-(trifluoromethyl)phenyl]sulfonyl}-*N*-[(2*R*)-2-hydroxy-3-methoxypropyl]pyridine-2-carboxamide;

3-amino-*N*-[2-oxo-2-(propan-2-ylamino)ethyl]-5-{[4-(trifluoromethyl)phenyl]sulfonyl}pyridine-2-carboxamide;

(3-amino-5-{[4-(trifluoromethyl)phenyl]sulfonyl}pyridin-2-yl)[3-hydroxy-3-(trifluoromethyl)azetidin-1-yl]methanone;

3-amino-5-{[2-fluoro-4-(trifluoromethyl)phenyl]sulfonyl}-*N*-[(3*R*)-tetrahydrofuran-3-ylmethyl]pyridine-2-carboxamide;

(3-amino-5-{[2-fluoro-4-(trifluoromethyl)phenyl]sulfonyl}pyridin-2-yl)[3-hydroxy-3-(trifluoromethyl)azetidin-1-yl]methanone;

3-amino-5-{[2-fluoro-4-(trifluoromethyl)phenyl]sulfonyl}-*N*-[(3*S*)-tetrahydrofuran-3-ylmethyl]pyridine-2-carboxamide;

3-amino-5-{[2-fluoro-4-(trifluoromethoxy)phenyl]sulfonyl}-*N*-[(3*S*)-tetrahydrofuran-3-ylmethyl]pyridine-2-carboxamide;

3-amino-*N*-[2-hydroxy-3-(2,2,2-trifluoroethoxy)propyl]-5-{[4-(trifluoromethyl)phenyl]sulfonyl}pyridine-2-carboxamide;

3-amino-*N*-(3-*tert*-butoxy-2-hydroxypropyl)-5-{[2-fluoro-4-(trifluoromethyl)phenyl]sulfonyl}pyridine-2-carboxamide;

[3-amino-5-(phenylsulfonyl)pyridin-2-yl][3-hydroxy-3-(trifluoromethyl)azetidin-1-yl]methanone;

{3-amino-5-[(3-fluorophenyl)sulfonyl]pyridin-2-yl}[3-hydroxy-3-(trifluoromethyl)azetidin-1-yl]methanone; and

3-amino-*N*-[(2*S*)-2-hydroxypropyl]-5-{[4-(trifluoromethoxy)phenyl]sulfonyl}pyridine-2-carboxamide.

[00293] Non-limiting examples of correctors include Lumacaftor (VX-809), 1-(2,2-difluoro-1,3-benzodioxol-5-yl)-*N*-{1-[(2*R*)-2,3-dihydroxypropyl]-6-fluoro-2-(1-hydroxy-2-methylpropan-2-yl)-1*H*-indol-5-yl}cyclopropanecarboxamide (VX-661), VX-983, GLPG2222, GLPG2665, GLPG2851, VX-152, VX-440, FDL169, FDL304, FD2052160, FD2035659 and PTI-801. Examples of correctors are also disclosed in US Applications 14/925,649, 14/926,727, 15/205,512, and 62/239475.

[00294] In one embodiment, the corrector(s) can be selected from the group consisting of:

Lumacaftor (VX-809);

1-(2,2-difluoro-1,3-benzodioxol-5-yl)-*N*-{1-[(2*R*)-2,3-dihydroxypropyl]-6-fluoro-2-(1-hydroxy-2-methylpropan-2-yl)-1*H*-indol-5-yl}cyclopropanecarboxamide (VX-661);

PTI-801;

VX-983;

GLPG2665;

VX-152;

VX-440;

FDL169;

FDL304;

FD2052160;

FD2035659;

3-[(2*R*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-7-methoxy-3,4-dihydro-2*H*-chromen-2-yl]benzoic acid;

3-[(2*R*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-3,4-dihydro-2*H*-chromen-2-yl]benzoic acid;

3-[(2*R*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-6-methyl-3,4-dihydro-2*H*-chromen-2-yl]benzoic acid;

3-[(2*R*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-7-methyl-3,4-dihydro-2*H*-chromen-2-yl]benzoic acid;

3-[(2*R*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-6-methoxy-3,4-dihydro-2*H*-chromen-2-yl]benzoic acid;

3-[(2*R*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-7-(difluoromethoxy)-3,4-dihydro-2*H*-chromen-2-yl]cyclohexanecarboxylic acid;

3-[(2*R*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-7-(difluoromethoxy)-3,4-dihydro-2*H*-chromen-2-yl]benzoic acid;

3-[(2*R*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-7-methoxy-3,4-dihydro-2*H*-chromen-2-yl]cyclohexanecarboxylic acid;

3-[(2*R*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-7-fluoro-3,4-dihydro-2*H*-chromen-2-yl]benzoic acid;

3-({3-[(2*R*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-7-methyl-3,4-dihydro-2*H*-chromen-2-yl]benzoyl}amino)-1-methylcyclopentanecarboxylic acid;

3-[(2*R*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-7-methyl-3,4-dihydro-2*H*-chromen-2-yl]-N-[(2*R*)-2,3-dihydroxypropyl]benzamide;

3-[(2*R*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-7-(2-methoxyethoxy)-3,4-dihydro-2*H*-chromen-2-yl]benzoic acid;

3-[(2*R*,4*R*)-7-(benzyloxy)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-3,4-dihydro-2*H*-chromen-2-yl]benzoic acid;

3-[(2*R*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-7-(2-fluoroethoxy)-3,4-dihydro-2*H*-chromen-2-yl]benzoic acid;

3-[(2*R*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-7-(trifluoromethyl)-3,4-dihydro-2*H*-chromen-2-yl]benzoic acid;

3-[(2*R*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-7-(trifluoromethyl)-3,4-dihydro-2*H*-chromen-2-yl]cyclohexanecarboxylic acid;

4-[(2*R*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-7-methoxy-3,4-dihydro-2*H*-chromen-2-yl]benzoic acid;

3-[(2*R*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-8-fluoro-3,4-dihydro-2*H*-chromen-2-yl]benzoic acid;

4-[(2*R*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-3,4-dihydro-2*H*-chromen-2-yl]benzoic acid;

4-[(2*R*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-7-(difluoromethoxy)-3,4-dihydro-2*H*-chromen-2-yl]benzoic acid;

rac-3-[(2*R*,4*S*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)tetrahydro-2*H*-pyran-2-yl]benzoic acid;

rac-4-[(2*R*,4*S*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)tetrahydro-2*H*-pyran-2-yl]benzoic acid;

3-[(2*S*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)tetrahydro-2*H*-pyran-2-yl]benzoic acid;

3-[(2*R*,4*S*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)tetrahydro-2*H*-pyran-2-yl]benzoic acid;

rac-3-[(2*R*,4*S*,6*S*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-6-phenyltetrahydro-2*H*-pyran-2-yl]benzoic acid;

3-[(2*S*,4*R*,6*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-6-phenyltetrahydro-2*H*-pyran-2-yl]benzoic acid;

3-[(2*R*,4*S*,6*S*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-6-phenyltetrahydro-2*H*-pyran-2-yl]benzoic acid;

4-[(2*R*,4*S*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)tetrahydro-2*H*-pyran-2-yl]benzoic acid;

3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid;

3-cyclobutyl-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid;

5-[(2*R*,4*R*)-4-{[(7*R*)-2,2-difluoro-7-methyl-6,7-dihydro-2*H*-furo[2,3-*f*][1,3]benzodioxole-7-carbonyl]amino}-7-methoxy-3,4-dihydro-2*H*-1-benzopyran-2-yl]pyrazine-2-carboxylic acid;

6-[(2*R*,4*R*)-4-{[(7*R*)-2,2-difluoro-7-methyl-6,7-dihydro-2*H*-furo[2,3-*f*][1,3]benzodioxole-7-carbonyl]amino}-7-(trifluoromethoxy)-3,4-dihydro-2*H*-1-benzopyran-2-yl]pyridine-3-carboxylic acid;

trans-4-[(2*S*,4*S*)-4-{[(7*R*)-2,2-difluoro-7-methyl-6,7-dihydro-2*H*-furo[2,3-*f*][1,3]benzodioxole-7-carbonyl]amino}-7-(trifluoromethoxy)-3,4-dihydro-2*H*-1-benzopyran-2-yl]cyclohexane-1-carboxylic acid;

6-[(2*R*,4*R*)-7-(difluoromethoxy)-4-{[(7*R*)-2,2-difluoro-7-methyl-6,7-dihydro-2*H*-furo[2,3-*f*][1,3]benzodioxole-7-carbonyl]amino}-3,4-dihydro-2*H*-1-benzopyran-2-yl]pyridine-3-carboxylic acid;

trans-4-[(2*S*,4*S*)-4-{[(7*R*)-2,2-difluoro-7-methyl-6,7-dihydro-2*H*-furo[2,3-*f*][1,3]benzodioxole-7-carbonyl]amino}-7-methoxy-3,4-dihydro-2*H*-1-benzopyran-2-yl]cyclohexane-1-carboxylic acid;

ethyl *trans*-4-[(2*S*,4*S*)-7-(difluoromethoxy)-4-{[(7*R*)-2,2-difluoro-7-methyl-6,7-dihydro-2*H*-furo[2,3-*f*][1,3]benzodioxole-7-carbonyl]amino}-3,4-dihydro-2*H*-1-benzopyran-2-yl]cyclohexane-1-carboxylate;

cis-4-[(2*R*,4*R*)-4-{[(7*R*)-2,2-difluoro-7-methyl-6,7-dihydro-2*H*-furo[2,3-*f*][1,3]benzodioxole-7-carbonyl]amino}-7-(trifluoromethoxy)-3,4-dihydro-2*H*-1-benzopyran-2-yl]cyclohexane-1-carboxylic acid;

trans-4-[(2*S*,4*S*)-7-(difluoromethoxy)-4-{[(7*R*)-2,2-difluoro-7-methyl-6,7-dihydro-2*H*-furo[2,3-*f*][1,3]benzodioxole-7-carbonyl]amino}-3,4-dihydro-2*H*-1-benzopyran-2-yl]cyclohexane-1-carboxylic acid;

1-[(2*R*,4*R*)-4-{[(7*R*)-2,2-difluoro-7-methyl-6,7-dihydro-2*H*-furo[2,3-*f*][1,3]benzodioxole-7-carbonyl]amino}-7-(trifluoromethoxy)-3,4-dihydro-2*H*-1-benzopyran-2-yl]cyclopropane-1-carboxylic acid;

trans-4-[(2*R*,4*R*)-4-{[(5*S*)-2,2-difluoro-5-methyl-6,7-dihydro-2*H*,5*H*-indeno[5,6-*d*][1,3]dioxole-5-carbonyl]amino}-7-(trifluoromethoxy)-3,4-dihydro-2*H*-1-benzopyran-2-yl]cyclohexane-1-carboxylic acid;

trans-4-[(2*R*,4*R*)-4-{[(5*S*)-2,2-difluoro-5-methyl-6,7-dihydro-2*H*,5*H*-indeno[5,6-*d*][1,3]dioxole-5-carbonyl]amino}-7-methoxy-3,4-dihydro-2*H*-1-benzopyran-2-yl]cyclohexane-1-carboxylic acid;

trans-4-[(2*R*,4*R*)-4-{[(7*R*)-2,2-difluoro-7-methyl-6,7-dihydro-2*H*-furo[2,3-*f*][1,3]benzodioxole-7-carbonyl]amino}-7-methoxy-3,4-dihydro-2*H*-1-benzopyran-2-yl]cyclohexane-1-carboxylic acid;

trans-4-[(2*R*,4*R*)-7-(difluoromethoxy)-4-{[(7*R*)-2,2-difluoro-7-methyl-6,7-dihydro-2*H*-furo[2,3-*f*][1,3]benzodioxole-7-carbonyl]amino}-3,4-dihydro-2*H*-1-benzopyran-2-yl]cyclohexane-1-carboxylic acid; and

trans-4-[(2*R*,4*R*)-4-{[(7*R*)-2,2-difluoro-7-methyl-6,7-dihydro-2*H*-furo[2,3-*f*][1,3]benzodioxole-7-carbonyl]amino}-7-(trifluoromethoxy)-3,4-dihydro-2*H*-1-benzopyran-2-yl]cyclohexane-1-carboxylic acid.

[00295] In one embodiment, the additional therapeutic agent is a CFTR amplifier. CFTR amplifiers enhance the effect of known CFTR modulators, such as potentiators and correctors. Examples of CFTR amplifiers are PTI130 and PTI-428. Examples of amplifiers are also disclosed in publications: WO2015138909 and WO2015138934.

[00296] In one embodiment, the additional therapeutic agent is a CFTR stabilizer. CFTR stabilizers enhance the stability of corrected CFTR that has been treated with a corrector, corrector/potentiator or other CFTR modulator combination(s). An example of a CFTR stabilizer is cavosonstat. Examples of stabilizers are also disclosed in publication: WO2012048181.

[00297] In one embodiment, the additional therapeutic agent is an agent that reduces the activity of the epithelial sodium channel blocker (ENaC) either directly by blocking the channel or indirectly by modulation of proteases that lead to an increase in ENaC activity (e.g., serine proteases, channel-activating proteases). Exemplary of such agents include camostat (a trypsin-like protease inhibitor), QAU145, 552-02, GS-9411, INO-4995, Aerolytic, amiloride, and VX-371. Additional agents that reduce the activity of the epithelial sodium channel blocker (ENaC) can be found, for example, in PCT Publication No. WO2009074575 and WO2013043720; and US Patent No. US8999976.

[00298] In one embodiment, the ENaC inhibitor is VX-371.

[00299] In one embodiment, the ENaC inhibitor is SPX-101 (S18).

[00300] In one embodiment, the present invention provides pharmaceutical compositions comprising a compound of the invention, or a pharmaceutically acceptable salt thereof, and one or more additional therapeutic agents. In a particular embodiment, the additional therapeutic agents are selected from the group consisting of CFTR modulators and CFTR amplifiers. In a further embodiment, the additional therapeutic agents are CFTR modulators. In one embodiment, the present invention provides pharmaceutical compositions comprising a compound of the invention, or a pharmaceutically acceptable salt thereof, one potentiator, and one or more additional correctors.

[00301] This invention also is directed to kits that comprise one or more compounds and/or salts of the invention, and, optionally, one or more additional therapeutic agents.

[00302] This invention also is directed to methods of use of the compounds, salts, compositions, and/or kits of the invention to, with or without one or more additional therapeutic agents, for example, modulate the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) protein, and treat a disease treatable by modulating the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) protein (including cystic fibrosis, Sjögren's syndrome, pancreatic insufficiency, chronic obstructive lung disease, and chronic obstructive airway disease).

EXAMPLES

CHEMICAL SYNTHETIC PROCEDURES

General

[00303] The compounds of the invention can be better understood in connection with the following synthetic schemes and methods which illustrate a means by which the compounds may be prepared.

[00304] The compounds of this invention can be prepared by a variety of synthetic procedures. Representative procedures are shown in, but are not limited to, Schemes 1-6. In Schemes 1-6, the variables R^1, R^2, R^3, R^4, R^5 and R^6 are as described in the Summary.

[00305] Optimum reaction conditions and reaction times for each individual step may vary depending on the particular reactants employed and substituents present in the reactants used. Unless otherwise specified, solvents, temperatures and other reaction conditions may be readily selected by one of ordinary skill in the art. Specific procedures are provided in the Synthetic Examples section. Reactions may be further processed in the conventional manner, e.g. by eliminating the solvent from the residue and further purified according to methodologies generally known in the art such as, but not limited to, crystallization, distillation, extraction, trituration and chromatography. Unless otherwise described, the starting materials and reagents are either commercially available or may be prepared by one skilled in the art from commercially available materials using methods described in the chemical literature.

[00306] Routine experimentations, including appropriate manipulation of the reaction conditions, reagents and sequence of the synthetic route, protection of any chemical functionality that may not be compatible with the reaction conditions, and deprotection at a suitable point in the reaction sequence of the method are included in the scope of the invention. Suitable protecting groups and the methods for protecting and deprotecting different substituents using such suitable protecting groups are well known to those skilled in the art; examples of which can be found in T. Greene and P. Wuts, Protecting Groups in Organic Synthesis (3rd ed.), John Wiley & Sons, NY (1999), which is incorporated herein by reference in its entirety. Synthesis of the compounds of the invention can be accomplished by methods analogous to those described in the synthetic schemes described hereinabove and in specific examples.

[00307] Starting materials, if not commercially available, can be prepared by procedures selected from standard organic chemical techniques, techniques that are analogous to the synthesis of known, structurally similar compounds, or techniques that are analogous to the above described schemes or the procedures described in the synthetic examples section.

[00308] When an optically active form of a compound is required, it can be obtained by carrying out one of the procedures described herein using an optically active starting material (prepared, for example, by asymmetric induction of a suitable reaction step), or by resolution of a mixture of the stereoisomers of the compound or intermediates using a standard procedure (such as chromatographic separation, recrystallization or enzymatic resolution).

[00309] Similarly, when a pure geometric isomer of a compound is required, it can be prepared by carrying out one of the above procedures using a pure geometric isomer as a starting material, or by resolution of a mixture of the geometric isomers of the compound or intermediates using a standard procedure such as chromatographic separation.

[00310] The compounds of the invention can be prepared from readily available starting materials using the following general methods and procedures. It will be appreciated that where typical or preferred process conditions (*i.e.* reaction temperatures, times, mole ratios of reactants, solvents, pressures, etc.) were given, other process conditions can also be used unless otherwise stated. Optimum reaction conditions may vary with the particular reactants or solvent used, but such conditions can be determined by one skilled in the art by routine optimization procedures.

[00311] The following methods are presented with details as to the preparation of a compound of the invention as defined hereinabove and the comparative examples. A compound of the invention may be prepared from known or commercially available starting materials and reagents by one skilled in the art of organic synthesis.

[00312] All reagents were of commercial grade and were used as received without further purification, unless otherwise stated. Commercially available anhydrous solvents were used for reactions conducted under inert atmosphere. Reagent grade solvents were used in all other cases, unless otherwise specified. Column chromatography was performed on silica gel 60 (35-70 μm). Thin layer chromatography was carried out using pre-coated silica gel F-254 plates (thickness 0.25 mm). ^{1}H NMR spectra were recorded on a Bruker Advance 300 NMR spectrometer (300 MHz) unless otherwise noted. Chemical shifts (δ) for ^{1}H NMR spectra were reported in parts per million (ppm) relative to tetramethylsilane (δ 0.00) or the appropriate residual solvent peak, i.e. $CHCl_3$ (δ 7.27), as internal reference. Multiplicities were given as singlet (s), doublet (d), triplet (t), quartet (q), quintuplet (quin), multiplet (m) and broad (br). Electrospray MS spectra were obtained on a Waters platform LC/MS spectrometer or with Waters Acquity H-Class UPLC coupled to a Waters Mass detector 3100 spectrometer. Columns used: Waters Acquity UPLC

BEH C18 1.7 µm, 2.1 mm ID x 50 mm L, Waters Acquity UPLC BEH C18 1.7 µm, 2.1 mm ID x 30 mm L, or Waters Xterra® MS 5 µm C18, 100 x 4.6 mm. The methods were using either MeCN/H_2O gradients (H_2O contains either 0.1% TFA or 0.1% NH_3) or Methanol/H_2O gradients (H_2O contains 0.05% TFA). Microwave heating was performed with a Biotage® Initiator. Electrospray MS spectra were obtained on Waters Acquity UPLC systems coupled to Waters SQD or SQD2 mass spectrometers. Columns used: Waters Acquity UPLC BEH C18 1.7 µm, 2.1 mm ID x 50 mm L or Waters Acquity UPLC BEH C18 1.7 µm, 2.1 mm ID x 30 mm L. The methods were using MeCN/H_2O gradients (both MeCN and H_2O contained either 0.1% formic acid or 0.05% NH_3).

[00313] For the compounds purified by preparative chromatography, an XSelect™ CSH Prep Guard Column, C18 19×10mm 5 µm (Waters) with an XSelect™ CSH Prep OBD Column, C18 19×100 mm 5 µm (Waters) and a gradient of 0.1% formic acid in water (A) and acetonitrile (B) at a flow rate of 20 mL/minute is used. Alternatively, an XBridge™ Prep Guard Column, C18 19×10 mm 5 µm (Waters) with a XBridge™ Prep OBD Column, C18 19×100 mm 5 µm (Waters) and a gradient of 0.5% NH_3 in water (A) and acetonitrile (B) at a flow rate of 20 mL/minute is used. After elution, the solvent was removed under vacuum to provide the product. For the compounds purified by preparative chromatography, an XBridge™ Prep Guard Column, C18 19×10 mm 5 µm (Waters) with a XBridge™ Prep OBD Column, C18 30×100 mm 5 µm (Waters) and a gradient of 0.1% formic acid in water (A) and acetonitrile (B) at a flow rate of 50 mL/minute were used. Alternatively, a gradient of 0.1% DEA in water (A) and acetonitrile (B) at a flow rate of 50 mL/minute was used on the same references of guard column and column. After elution, the solvent was removed under vacuum to provide the dry product.

[00314] Alternatively, compounds were purified by automated reversed phase HPLC, using a Phenomenex® Luna® C8(2), 5 µm, 100Å, 50 × 30 mm, with a SecurityGuard™ 15 × 30 mm guard column, and a gradient of acetonitrile (A) and 0.1% trifluoroacetic acid in water (B), at a flow rate of 40 mL/min (0 - 1.0 minute 10% A, 1.0 - 9.0 minutes linear gradient 10 - 100% A, 9.0 - 9.5 minutes 100% A, 9.5 - 10.0 minutes linear gradient 100 - 10% A). After elution, solvent was removed under vacuum to provide the pure product.

[00315] Racemic mixtures were separated on an Agilent HP1100 system with UV detection. Column used: Chiralpak® IA (10 x 250 mm, 5 µm). Solvents used: *i*PrOH and *t*BME.

Enantiomeric purity was determined on an Agilent HP1100 system with UV detection. Column used: Chiralpak IA (4.6x250 mm, 5µm). Solvents used: iPrOH and tBME.

[00316] List of abbreviations used in the experimental section:

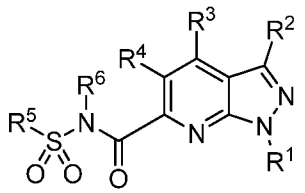
Abbreviation	Definition
Bn	benzyl
Boc	*tert*-butoxycarbonyl
Et	ethyl
Me	methyl
Ph	phenyl
Pr	propyl
Tf	trifluoromethanesulfonyl
OTf	trifluormethanesulfonate
DCM	dichloromethane
MeCN	acetonitrile
DMA	*N,N*-dimethylacetamide
DMF	*N,N*-dimethylformamide
AcOH or HOAc	acetic acid
eq or equiv	equivalents
TFA	trifluoroacetic acid
THF	tetrahydrofuran
NMR	nuclear magnetic resonance
DMSO	dimethyl sulfoxide
LC/MS or LCMS	liquid chromatography-mass spectrometry
EtOAc	ethyl acetate
EtOH	ethanol
MeOH	methanol
tBuOH or *t*-BuOH	*tert*-butanol
*t*BME or MTBE	*tert*-butyl methyl ether
s	singlet

Abbreviation	Definition
br s	broad singlet
d	duplet
dd	double duplet
m	multiplet
min	minute
h	hours
mL	milliliter
µL	microliter
g	gram
mg	milligram
kg	kilogram
atm	atmosphere
w/w	weight/weight
RT	room(ambient) temperature
NEt_3	triethylamine
BOP	(benzotriazol-yloxy)tris(dimethylamino)phosphonium hexafluorophosphate
DIPEA	diisopropylethylamine
DMAP	dimethylaminopyridine
EDC	*N*-ethyl-*N'*-(3-dimethylaminopropyl)carbodiimide
mmol	millimoles
HPLC	high pressure liquid chromatography
MS	mass spectrum
NMR	nuclear magnetic resonance
TLC	thin layer chromatography
NMP	*N*-methylpyrrolidone
ppm	parts per million
psi	pounds per square inch
$Pd(OAc)_2$	palladium(II) acetate

Abbreviation	Definition
Xantphos	4,5-bis(diphenylphosphino)-9,9-dimethylxanthene
SM	starting material
Cpd	compound
Int	intermediate
MW	molecular weight
Mes	molecular weight measured
NA	not active
$Pd(dppf)Cl_2$	[1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II)
$Pd(dppf)Cl_2•CH_2Cl_2$ or $Pd(dppf)Cl_2•DCM$	[1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) complex with dichloromethane
µm	micrometer
*i*PrOH	*iso*-propanol
DBU	1,8-diazabicycloundec-7-ene
DPPA	diphenylphosphoryl azide
LiHMDS	lithium hexamethyldisilazide or lithium bis(trimethylsilyl)amide
rac-BINAP	*rac*-1,1′-binaphthyl-2,2′-diamine
TfOH	trifluoromethanesulfonic acid
Tf_2O	trifluoromethanesulfonic anhydride
XPhos	2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl
XPhos Pd G1	(2-dicyclohexylphosphino-2′,4′,6′-triisopropyl-1,1′-biphenyl)[2-(2-aminoethyl)phenyl)]palladium(II) chloride
K_2CO_3	potassium carbonate
$MgSO_4$	magnesium sulfate
$NaHCO_3$	sodium hydrogencarbonate or sodium bicarbonate
Na_2CO_3	sodium carbonate

Abbreviation	Definition
Na_2SO_4	sodium sulfate
CO	carbon monoxide
NaCl	sodium chloride
NaH	sodium hydride
LiOH	lithium hydroxide
Pd(amphos)Cl_2	bis(di-*tert*-butyl(4-dimethylaminophenyl)phosphine)dichloropalladium(II)
SPhos	2-dicyclohexylphosphino-2′,6′-dimethoxybiphenyl

SYNTHETIC PREPARATION OF THE COMPOUNDS OF THE INVENTION

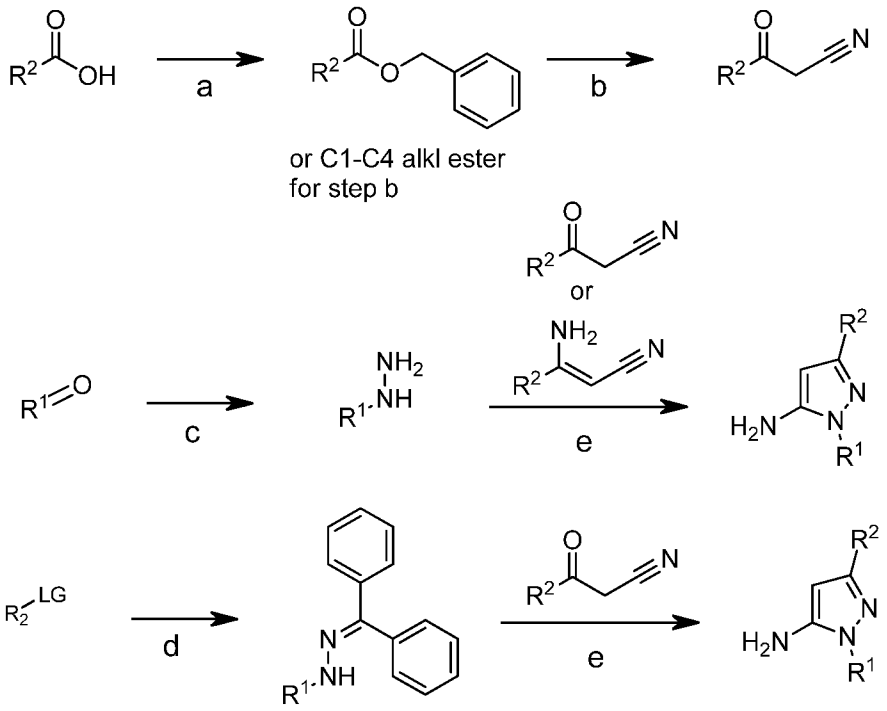


(I)

General synthetic routes

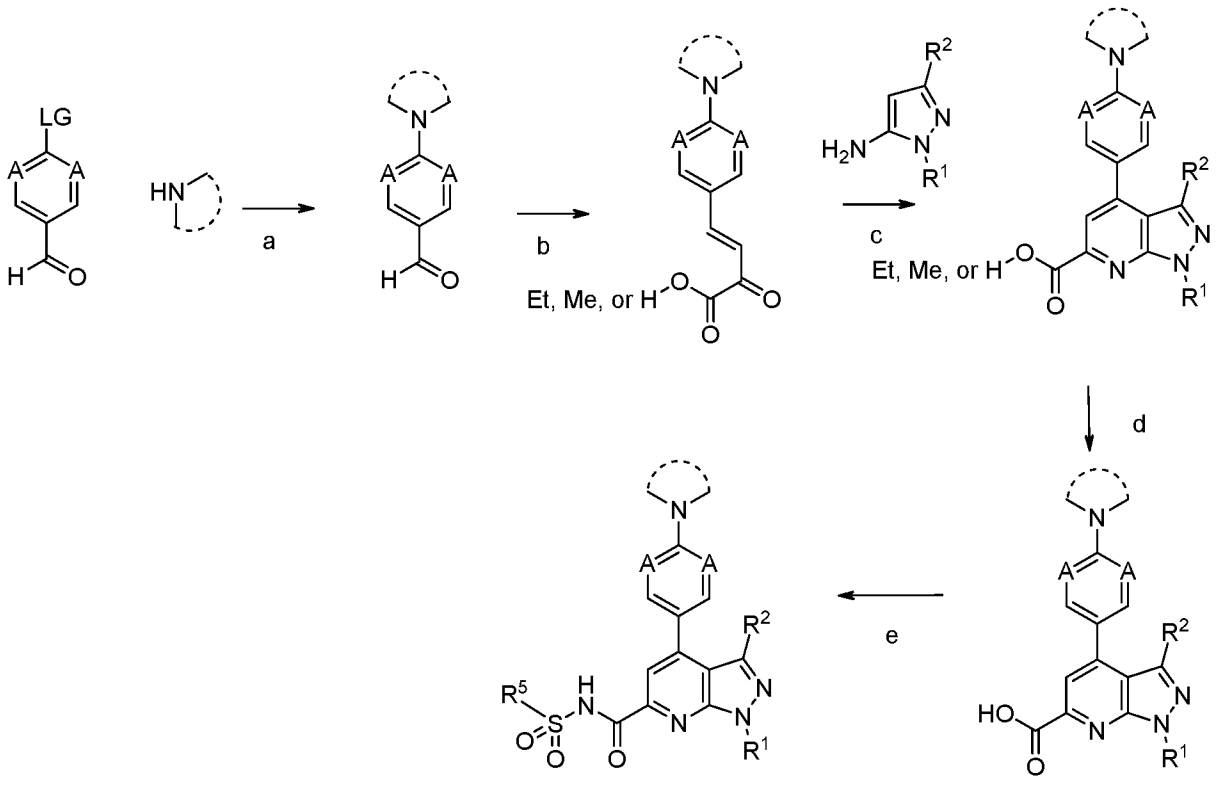
[00317] The compounds of the invention and the comparative examples can be produced according to the following schemes.

Scheme 1: General synthetic access to aminopyrazoles



a) method A; b) method B; c) methods C1-C4; d) method D; e) methods E1-E6

Scheme 2: Synthesis of final compounds by general route A

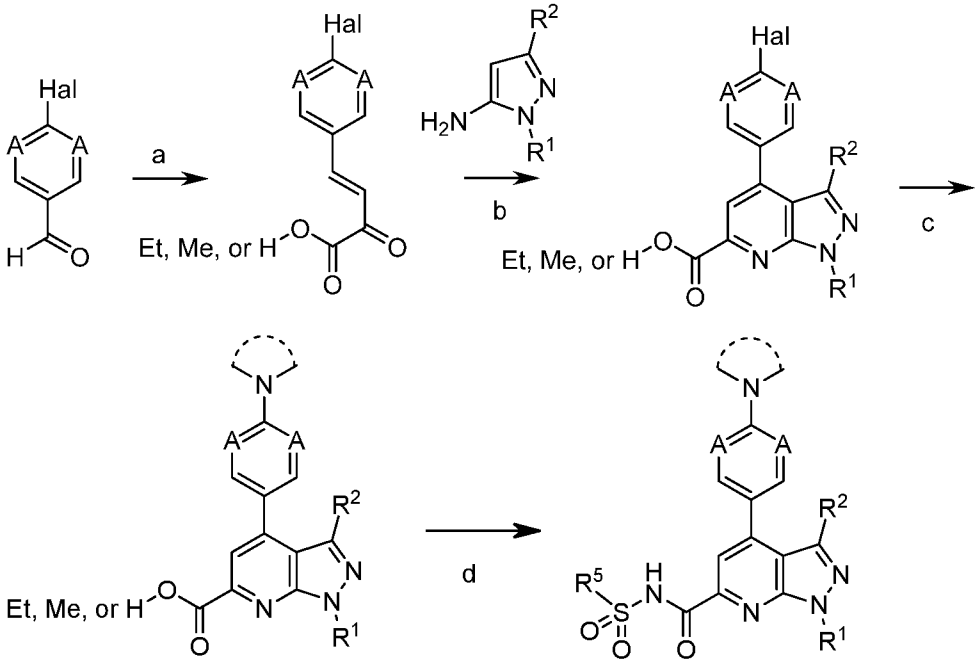


LG= F, Cl, Br

A=CH or N

a) method F; b) methods G1-G2; c) methods I1, J2; d) method J1; e) methods Y1-Y10

Scheme 3: Synthesis of final compounds by general route B

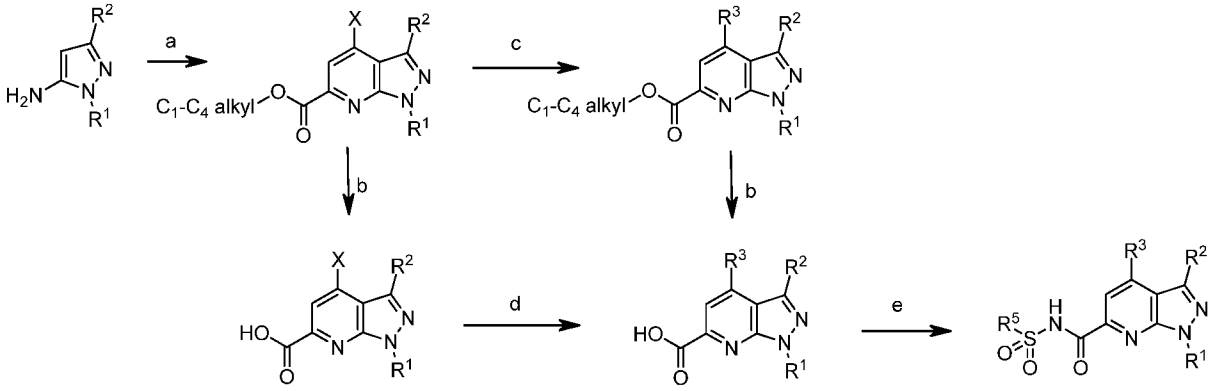


Hal= Cl, Br

A=CH, N

a) methods G1, G2 ; b) methods I1, J2 ; c) methods I10, J5 ; d) methods Y1-Y10

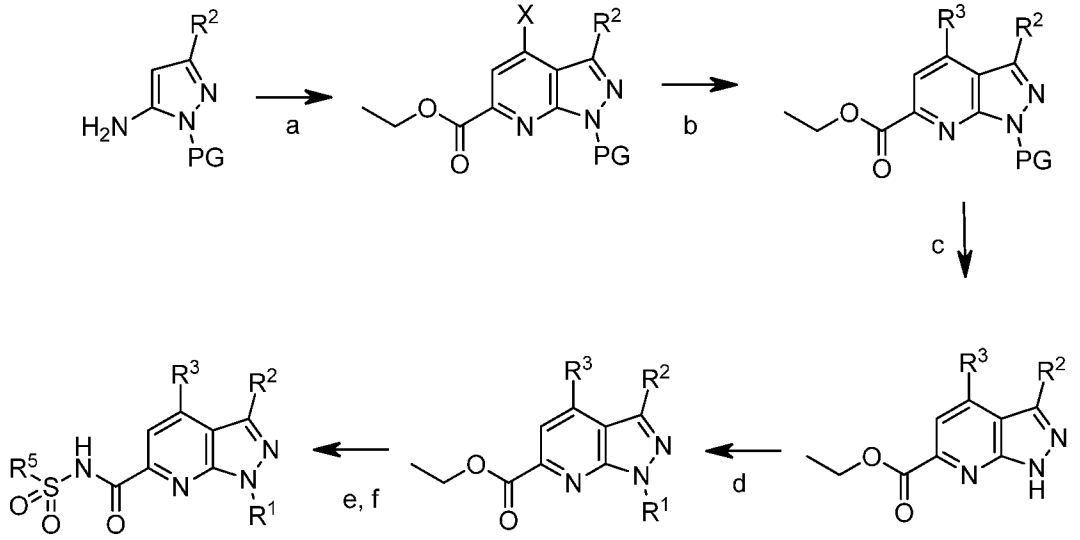
Scheme 4: Synthesis of final compounds by general route C



X = Cl, Br, OTf, OH

a) methods H1-H3, Specific examples HP12 and HP14; b) method J1, J1A; c) methods I2, I3, I14, J13, J14 ; d) methods J3, J4, J10; e) methods Y1-Y10

Scheme 5: Synthesis of final compounds by general route D



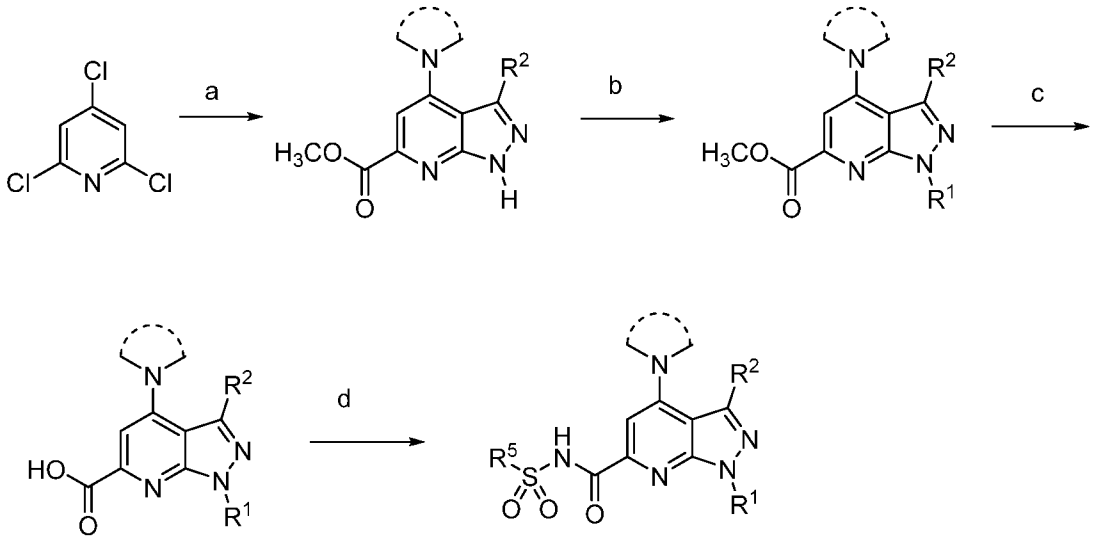
PG = protecting group (i.e., dimethoxybenzyl)

X = Cl, Br, OTf

a) method H3 and Specific example HP14; b) methods I2, I3, I14; c) method I15;

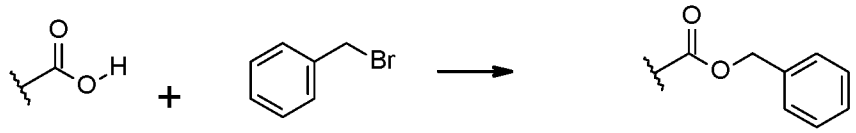
d) methods I4-I7, I16; e) method J1, J1A; f) methods Y1-Y10

Scheme 6: Synthesis of final compounds by general route E.



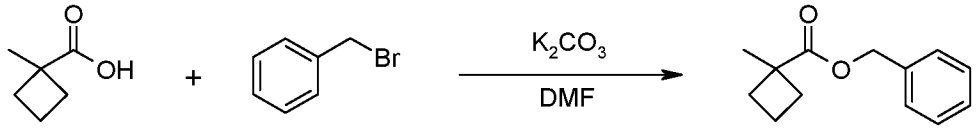
a) Specific example E509; b) methods I4-I7, I16; c) method J1, J1A;
d) methods Y1, Y4, Y5, Y8

Method A: Synthesis of benzyl esters



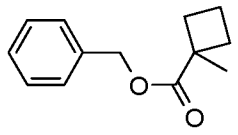
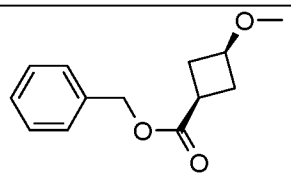
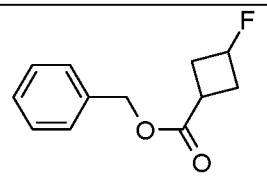
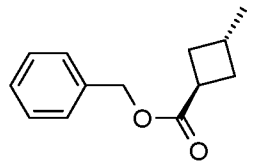
[00318] To a solution of the carboxylic acid (1.0 equiv) in either dry DMF or dry acetonitrile is added K_2CO_3 (1.3 equiv) followed by benzyl bromide (1.1 equiv). The reaction mixture is heated at a temperature ranging from RT to 85 °C for 2-4 h and then partitioned between brine and either ethyl acetate or dichloromethane. The organic layer is separated, washed with brine and saturated ammonium chloride, dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting residue is purified by flash chromatography on silica gel (eluent system: heptane/ethyl acetate) to afford the titled compound.

Illustrative synthesis of intermediate BE01: 1-Methyl-cyclobutanecarboxylic acid benzyl ester

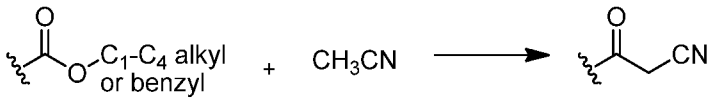


[00319] To a solution of 1-methylcyclobutanecarboxylic acid (CAS: 32936-76-8, 0.5 g, 4.38 mmol, 1.0 equiv) in dry DMF was added K_2CO_3 (0.787 g, 5.69 mmol, 1.3 equiv) followed by benzyl bromide (CAS: 100-39-0, 0.57 mL, 4.82 mmol, 1.1 equiv). The reaction mixture was stirred at RT for 2.5 h and then diluted with ethyl acetate and brine. The organic layer was separated, washed with a saturated solution of ammonium chloride and brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting residue was purified by flash chromatography on silica gel (eluent system: heptane/ethyl acetate gradient from 100/0 to 90/10) to afford the titled compound.

Table I. List of benzyl esters

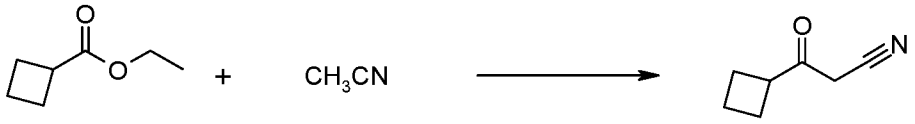
Int.	Structure	Name	SM	method	MW
BE01		1-Methyl-cyclobutanecarboxylic acid benzyl ester	32936-76-8	A, Specific example	204
BE02		3-Methoxy-cyclobutanecarboxylic acid benzyl ester	552849-35-1	A	220
BE03		3-Fluoro-cyclobutanecarboxylic acid benzyl ester	122665-96-7	A	208
BE04		3-Methyl-cyclobutanecarboxylic acid benzyl ester	87863-09-0	A	204

Method B: Cyanoketone formation



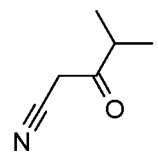
[00320] A flame-dried round bottom flask is cooled down to RT under nitrogen. A solution of 1 M LiHMDS in THF (1.5 equiv) is introduced into the flask, and then it is cooled down to -78 °C (acetone/dry ice bath). Dry MeCN (from 1.5 to 1.7 equiv) is then added dropwise under nitrogen, and the reaction mixture is stirred for 30 min at -78 °C. At this point a solution of ester (1.0 equiv) in dry THF is added dropwise, and then the reaction mixture is stirred at -78 °C for 1-2 h. The reaction mixture is quenched with cold H_2O, partitioned between ethyl acetate (or diethyl ether) and H_2O. The organic layer is separated, and the aqueous layer is extracted with ethyl acetate (or diethyl ether). The aqueous fraction is then acidified to pH=1 with 2 N HCl and extracted with ethyl acetate (or diethyl ether). The combined organic layers are then washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to afford the titled compound which is used as such or purified by flash chromatography on silica gel.

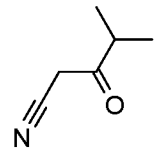
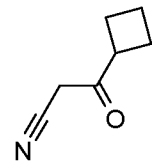
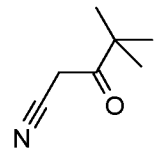
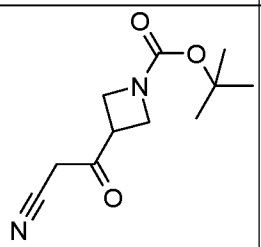
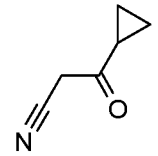
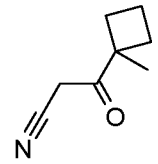
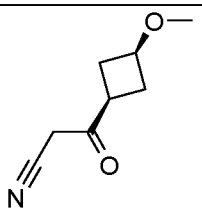
Illustrative synthesis of CK01: Cyclobutyl-3-oxo-propionitrile

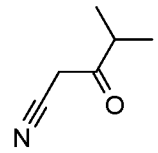
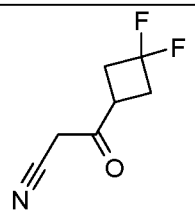
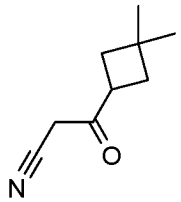
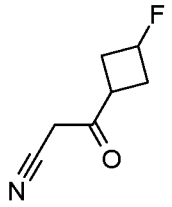
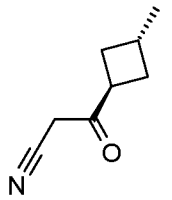


[00321] A 1 L 4 neck round bottom flask was equipped with 2 dropping funnels and a septum on top of the apparatus. The whole system was flame-dried (heat gun) for 10 minutes under vacuum and then cooled down to RT under a positive stream of nitrogen (balloon). A low-temperature thermometer was adapted under a positive stream of nitrogen, then a 1 N LiHMDS solution in THF (468.0 mL, 468.0 mmol, 1.5 equiv) was cannulated into the flask using a positive stream of nitrogen. The solution was cooled down to -78 °C (dry ice/acetone cooling bath) as confirmed with the thermometer. Dry MeCN (24.4 mL, 468.0 mmol, 1.5 equiv) was added via syringe into the first dropping funnel, and then added dropwise (over 20 min) into the reaction mixture. After the end of the addition, the mixture was stirred at -78 °C for 1 h. At this point, cyclobutanecarboxylic acid ethyl ester (CAS: 14924-53-9, 43.1 mL, 312.1 mmol, 1.0 equiv) as a solution in dry THF (106 mL) was introduced into the second dropping funnel. This solution was slowly added over 2 h into the reaction mixture at -78 °C. The mixture was stirred at -78 °C for 2 h. The reaction mixture was poured into 300 mL of cold water, stirred for 30 min and allowed to warm to RT. The mixture was then partitioned between ethyl acetate and H_2O. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (3 × 300 mL). The combined organic phases were discarded. The aqueous layer was then acidified with 100 mL of 2 N HCl, then extracted with ethyl acetate (3 × 300 mL), washed with 50 mL of brine, dried over $MgSO_4$, filtered and concentrated in vacuo to afford the titled compound which was used without further purification.

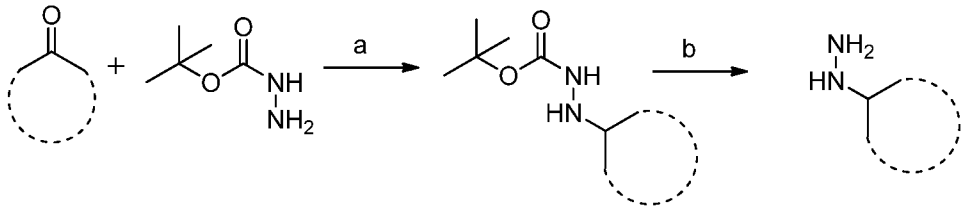
Table II. List of cyanoketones

Int.	Structure	Name	SM	method	MW	Mes
29509-06-6		4-Methyl-3-oxo-pentanenitrile			111	

Int.	Structure	Name	SM	method	MW	Mes
29509-06-6		4-Methyl-3-oxo-pentanenitrile			111	
CK01, 118431-89-3		3-Cyclobutyl-3-oxo-propionitrile	14924-53-9	B, Specific example	123	
59997-51-2		4,4-Dimethyl-3-oxo-pentanenitrile			125	
887594-13-0		3-(2-Cyano-acetyl)-azetidine-1-carboxylic acid *tert*-butyl ester			224	
118431-88-2		3-Cyclopropyl-3-oxo-propionitrile			109	
CK02		3-(1-Methyl-cyclobutyl)-3-oxo-propionitrile	BE01	B	137	138
CK03		3-(*cis*-3-Methoxy-cyclobutyl)-3-oxo-propionitrile	BE02	B	153	

Int.	Structure	Name	SM	method	MW	Mes
29509-06-6		4-Methyl-3-oxo-pentanenitrile			111	
1234616-26-2		3-(3,3-Difluoro-cyclobutyl)-3-oxo-propionitrile			159	
CK04		3-(3,3-Dimethyl-cyclobutyl)-3-oxo-propionitrile	3854-83-9	B	151	
CK05		3-(3-Fluoro-cyclobutyl)-3-oxo-propionitrile	BE03	B	141	
CK06		3-(*trans*-3-Methyl-cyclobutyl)-3-oxo-propionitrile	BE04	B	137	

Method C: Hydrazine formation



a) methods C1, C2; b) methods C3,C4

Method C1: Reductive amination

[00322] To a solution of ketone (1 equiv) and *tert*-butyl carbazate (CAS: 870-46-2, 1.0 equiv) in anhydrous dichloromethane at 0 °C is added acetic acid (2.0 equiv) and sodium triacetoxyborohydride (CAS: 56553-60-7, 3.0 equiv). The reaction mixture is warmed up to RT and stirred for 1h to several days (up to 8). The reaction mixture is then basified with a solution of 2 M sodium hydroxide and a saturated solution of sodium hydrogencarbonate. The two phases are separated, and the aqueous phase is extracted with dichloromethane. The combined organic phases are washed with a saturated solution of sodium hydrogencarbonate and brine, dried over $MgSO_4$, filtered and concentrated in vacuo to afford the *tert*-butoxy carbonyl hydrazine which is used as such or purified by flash chromatography on silica gel.

Method C2: Reductive amination

[00323] To the ketone (1 equiv) in anhydrous methanol at RT is added *tert*-butyl carbazate (CAS: 870-46-2, 1.0 equiv). The reaction mixture is stirred for 20 minutes at RT, then acetic acid (3.0 equiv) and sodium cyanoborohydride (CAS: 25895-60-7, 1.5 equiv) are added. The reaction mixture is stirred at RT for 1 h to several days (up to 8). The reaction mixture is then basified with a solution of 2 M sodium hydroxide and a saturated solution of sodium hydrogencarbonate. The two phases are separated, and the aqueous phase is extracted with dichloromethane. The combined organic phases are washed with a saturated solution of sodium hydrogencarbonate and brine, dried over $MgSO_4$, filtered and concentrated in vacuo to afford the *tert*-butoxy carbonyl hydrazine which is used as such or purified by flash chromatography on silica gel.

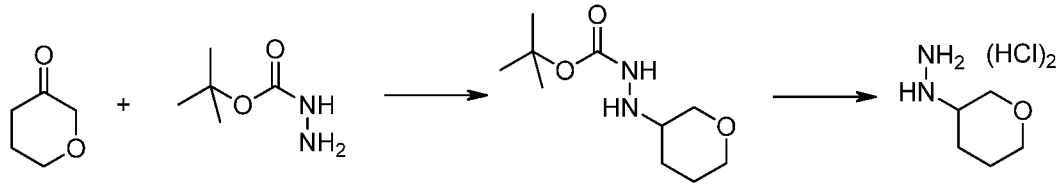
Method C3: tert-Butoxy carbonyl-deprotection

[00324] To a solution of a *tert*-butoxy carbonyl hydrazine intermediate from Methods C1 or C2 in anhydrous dichloromethane at RT is added 4 M HCl in dioxane (20 equiv). The reaction mixture is stirred at RT until the reaction is finished. The solids are collected by filtration, washed twice with diethyl ether, and dried in vacuo to afford the hydrazine which is used as such.

Method C4: tert-Butoxy carbonyl-deprotection

[00325] A *tert*-butoxy carbonyl hydrazine intermediate from Methods C1 or C2 is stirred at RT in a 1:1 mixture of dichloromethane and trifluoroacetic acid until the reaction is finished. The reaction mixture is concentrated in vacuo. The residue is taken up three times with toluene and concentrated in vacuo to afford the hydrazine which is used as such.

Illustrative synthesis of H01: (Tetrahydro-pyran-3-yl)-hydrazine di-hydrochloride salt



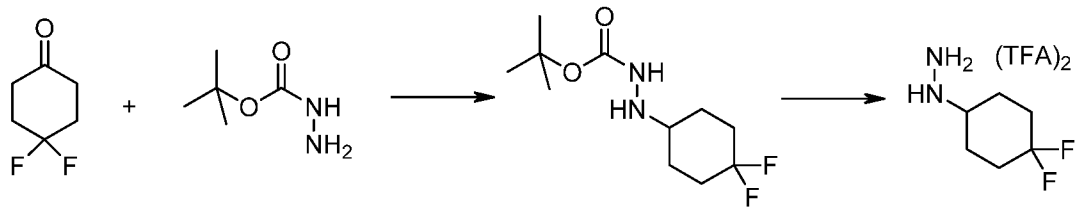
[00326] *Step1: tert-butyl N-(tetrahydropyran-3-ylamino)carbamate*

[00327] To a solution of dihydro-2*H*-pyran-3(4*H*)-one (CAS: 23462-75-1, 0.6 g, 5.99 mmol, 1.0 equiv) and *tert*-butyl carbazate (CAS: 870-46-2, 0.792 g, 5.99 mmol, 1.0 equiv) in anhydrous dichloromethane (20 mL) at 0 °C was added acetic acid (0.685 mL, 11.98 mmol, 2.0 equiv) and sodium triacetoxyborohydride (CAS: 56553-60-7, 3.81 g, 17.97 mmol, 3.0 equiv). The reaction mixture was warmed up to RT and stirred for 24 h. The reaction mixture was then basified with a solution of 2 M sodium hydroxide (45 mL) and a saturated solution of sodium hydrogencarbonate (30 mL). The two phases were separated, and the aqueous phase was extracted with dichloromethane. The combined organic phases were washed with a saturated solution of sodium hydrogencarbonate and brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting residue was purified by flash chromatography on silica gel (eluent system: heptane/ethyl acetate 70/30) to afford *tert*-butyl 2-(oxan-3-yl)hydrazine-1-carboxylate.

[00328] *Step 2: (Tetrahydro-pyran-3-yl)-hydrazine di-hydrochloride salt*

[00329] To a solution of *tert*-butyl 2-(oxan-3-yl)hydrazine-1-carboxylate from Step 1 (0.534 g, 2.46 mmol, 1 equiv) in anhydrous dichloromethane (1.74 mL) at RT was added 4 M HCl in dioxane (12.34 mL, 49.38 mmol, 20 equiv). The reaction mixture was stirred at RT overnight, and then the solid was collected by filtration. The solid was washed twice with diethyl ether and dried in vacuo to afford the titled compound, H01.

Illustrative synthesis of H02: 4,4-Difluoro-cyclohexyl)-hydrazine bis(trifluoroacetate)



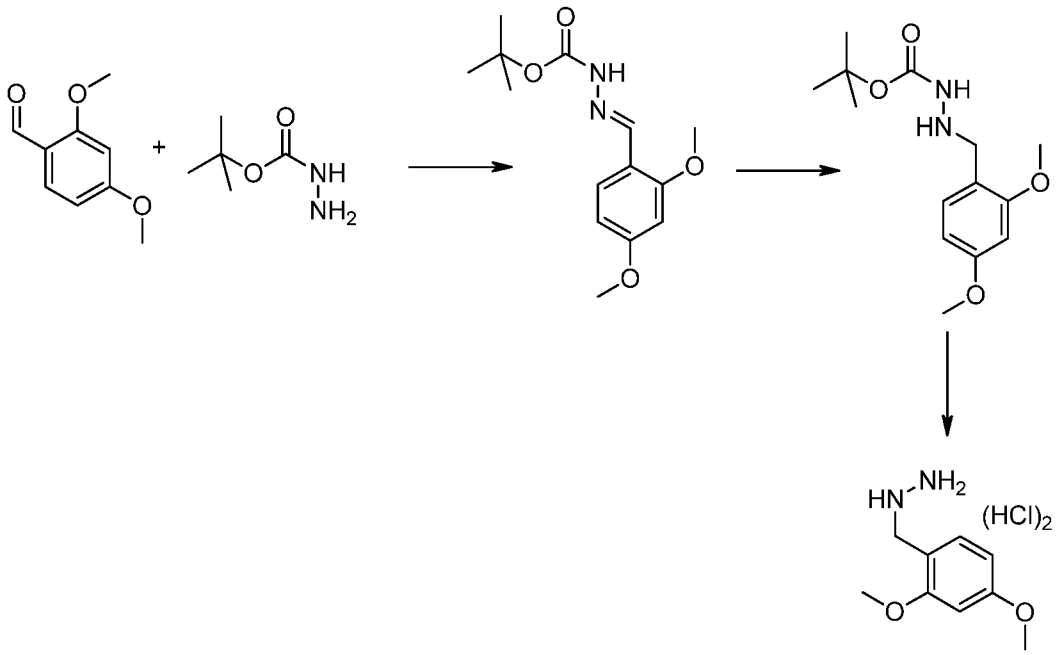
[00330] *Step 1: tert-butyl N-[(4,4-difluorocyclohexyl)amino]carbamate*

[00331] To 4,4-difluorocyclohexanone (CAS: 22515-18-0, 0.4 g, 2.98 mmol, 1.0 equiv) in anhydrous methanol (8.5 mL) at RT was added *tert*-butyl carbazate (CAS: 870-46-2, 0.394 g, 2.98 mmol, 1.0 equiv). The reaction mixture was stirred for 20 minutes at RT, and then acetic acid (0.51 mL, 8.95 mmol, 3.0 equiv) and sodium cyanoborohydride (CAS: 25895-60-7, 0.281 g, 4.47 mmol, 1.5 equiv) were added. The reaction mixture was stirred at RT overnight. The reaction mixture was then basified with a solution of 2 M sodium hydroxide (22 mL) and a saturated solution of sodium hydrogencarbonate (15 mL). The two phases were separated, and the aqueous phase was extracted with dichloromethane. The combined organic phases were washed with a saturated solution of sodium hydrogencarbonate and brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting residue was purified by flash chromatography on silica gel (eluent system: heptane/ethyl acetate gradient from 100/0 to 50/50) to afford *tert*-butyl 2-(4,4-difluorocyclohexyl)hydrazine-1-carboxylate.

[00332] *Step 2: 4,4-Difluoro-cyclohexyl)-hydrazine bis(trifluoroacetate)*

[00333] The *tert*-butyl 2-(4,4-difluorocyclohexyl)hydrazine-1-carboxylate intermediate from Step 1 (0.2 g, 0.8 mmol, 1 equiv) was stirred at RT in a 1:1 mixture of dichloromethane (0.65 mL) and trifluoroacetic acid (0.65 mL) for 1.5 h. The reaction mixture was concentrated in vacuo. The residue was taken up three times with toluene and concentrated in vacuo to afford the titled compound, H02.

Synthesis of H04: (2,4-Dimethoxy-benzyl)-hydrazine di-hydrochloride salt



[00334] *Step 1: tert-butyl N-[(E)-(2,4-dimethoxyphenyl)methyleneamino]carbamate*

[00335] To 2,4-dimethoxybenzaldehyde (CAS: 613-45-6, 37.82 g, 228 mmol, 1.0 equiv) in methanol at RT was added *tert*-butyl carbazate (CAS: 870-46-2, 30.08 g, 228 mmol, 1.0 equiv) and $MgSO_4$ (18.9 g). The reaction mixture was stirred at RT overnight. The reaction mixture was filtered through a pad of diatomaceous earth. The solids were washed with dichloromethane, and the filtrate was concentrated in vacuo. The residue was taken up in diethyl ether (120 mL) and stirred at RT. The resulting slurry was filtered. The solid was washed three times with diethyl ether and dried in vacuo to afford *tert*-butyl 2-[(2,4-dimethoxyphenyl)methylidene]hydrazine-1-carboxylate.

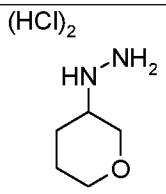
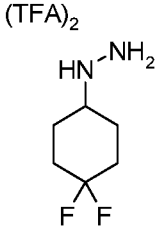
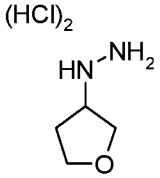
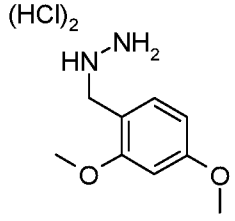
[00336] *Step 2: tert-butyl N-[(2,4-dimethoxyphenyl)methylamino]carbamate*

[00337] A 2-L round bottom flask under nitrogen atmosphere was charged with methanol (1.3 L), 10% palladium on carbon (13.6g), and *tert*-butyl 2-[(2,4-dimethoxyphenyl)methylidene]hydrazine-1-carboxylate from Step 1 (68.41 g, 228 mmol, 1 equiv). The reaction mixture was placed under vacuum then filled with hydrogen and kept under a hydrogen atmosphere (balloon). The reaction mixture was stirred at RT for 5 h. The reaction mixture was filtered through a pad of diatomaceous earth. The solids were washed with methanol, and the filtrate was concentrated in vacuo. The resulting residue was purified by flash chromatography on silica gel (eluent system: heptane/ethyl acetate, gradient from 50/50 to 40/60) to afford *tert*-butyl 2-[(2,4-dimethoxyphenyl)methyl]hydrazine-1-carboxylate.

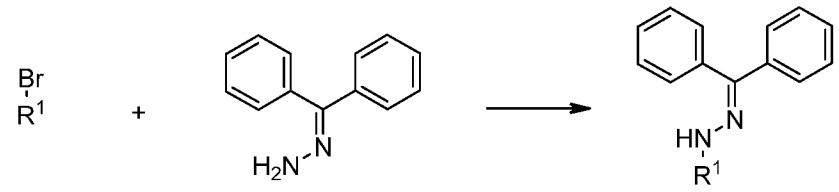
[00338] *Step 3: (2,4-Dimethoxy-benzyl)-hydrazine di-hydrochloride salt*

[00339] A 2-L round bottom flask was charged with *tert*-butyl 2-[(2,4-dimethoxyphenyl)methyl]hydrazine-1-carboxylate from Step 2 (59.8 g, 211 mmol, 1.0 equiv), then a solution of 4 M HCl in dioxane (600mL, 2400 mmol, 11.35 equiv) was added. The reaction mixture was stirred at RT overnight. The reaction mixture was filtered. The solid was washed three times with diethyl ether and dried in vacuo to afford the titled compound, H04.

Table III. List of Hydrazines

Int.	Structure	Name	SM	method	MW	Mes
H01		(Tetrahydro-pyran-3-yl)-hydrazine di-hydrochloride salt	23462-75-1	C1, C3 Specific example	116	
H02		(4,4-Difluoro-cyclohexyl)-hydrazine di–trifluoroacetic acid salt	22515-18-0	C2, C4 Specific example	150	
H03		(Tetrahydro-furan-3-yl)-hydrazine di-hydrochloride salt	22929-52-8	C2, C3	102	
H04		(2,4-Dimethoxy-benzyl)-hydrazine di-hydrochloride salt	613-45-6	Specific example	182	183

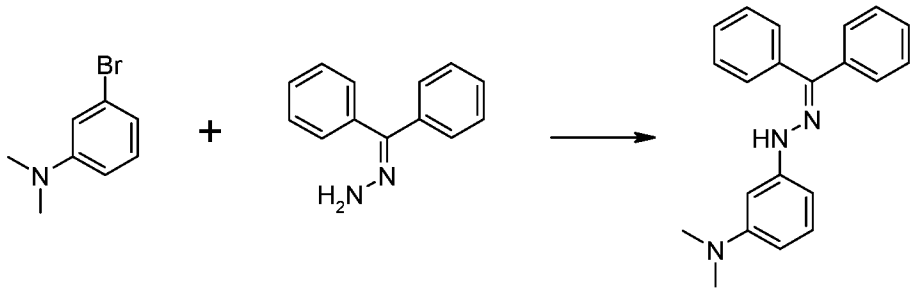
Method D: Aryl hydrazones formation



R^1 = phenyl or 5-6 membered monocyclic heteroaryl

[00340] An aryl bromide (1.05 equiv), benzophenone hydrazone (CAS: 5350-57-2, 1.0 equiv) and *rac*-BINAP (CAS: 98327-87-8, 0.06 equiv) are introduced in a round bottom flask at RT and suspended in anhydrous toluene. The slurry is purged with argon (bubbling). Then palladium(II) acetate (CAS: 3375-31-3, 0.02 equiv) and sodium *tert*-butoxide (CAS: 865-48-5, 1.3 equiv) are added, and the resulting slurry is purged with argon again. The reaction mixture is heated at 100 °C until the reaction is finished. The reaction mixture is cooled down to RT and filtered through a pad of diatomaceous earth. Solids were washed with ethyl acetate, and the filtrate is concentrated in vacuo. The titled compound is obtained from the crude filtrate either by precipitation from a suitable solvent or by purification by flash chromatography on silica gel (eluent system: heptane/ethyl acetate).

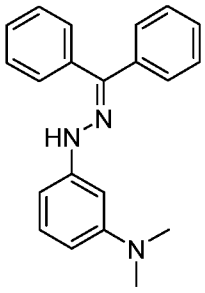
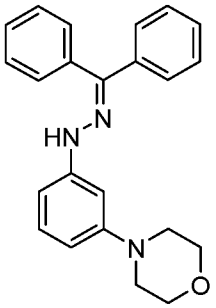
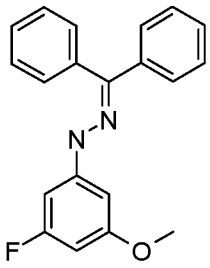
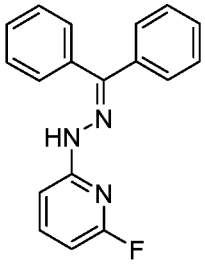
Illustrative synthesis of ArH01: [3-(N'-Benzhydrylidene-hydrazino)-phenyl]-dimethyl-amine

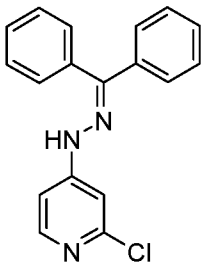


[00341] 3-Bromo-*N*,*N*-dimethylaniline (CAS:16518-62-0, 18.55 mL, 130 mmol, 1.05 equiv), benzophenone hydrazone (CAS: 5350-57-2, 24.29 g, 124 mmol, 1.0 equiv) and *rac*-BINAP (CAS: 98327-87-8, 4.62g, 7.43 mmol, 0.06 equiv) were combined in a round bottom flask at RT and suspended in anhydrous toluene (80 mL). The slurry was purged with argon (bubbling), and then palladium(II) acetate (CAS: 3375-31-3, 0.556 g, 2.48 mmol, 0.02 equiv) and sodium *tert*-butoxide (CAS: 865-48-5, 15.46 g, 161 mmol, 1.3 equiv) were added. The resulting slurry was purged with argon again, and the reaction mixture was heated at 100 °C for 1.5 h. The reaction

mixture was cooled down to RT and filtered through a pad of diatomaceous earth. The solids were washed with ethyl acetate, and the filtrate was concentrated in vacuo. The residue was taken up in diethyl ether, and stirred at RT. The resulting slurry was filtered. The collected solid was washed twice with diethyl ether and dried in vacuo to afford the titled compound.

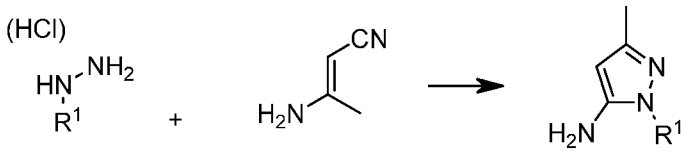
Table IV. List of Arylhydrazones

Int.	Structure	Name	SM	method	MW	Mes
ArH01		[3-(*N'*-Benzhydrylidene-hydrazino)-phenyl]-dimethyl-amine	16518-62-0	D Specific example	315	316
ArH02		*N*-Benzhydrylidene-*N'*-(3-morpholin-4-yl-phenyl)-hydrazine	197846-82-5	D	357	358
ArH03		*N*-Benzhydrylidene-*N'*-(3-fluoro-5-methoxy-phenyl)-hydrazine	29578-39-0	D	320	321
ArH04		*N*-Benzhydrylidene-*N'*-(6-fluoro-pyridin-2-yl)-hydrazine	144100-07-2	D	291	292

Int.	Structure	Name	SM	method	MW	Mes
ArH05		*N*-Benzhydrylidene-*N'*-(2-chloro-pyridin-4-yl)-hydrazine	73583-37-6	D	308	309

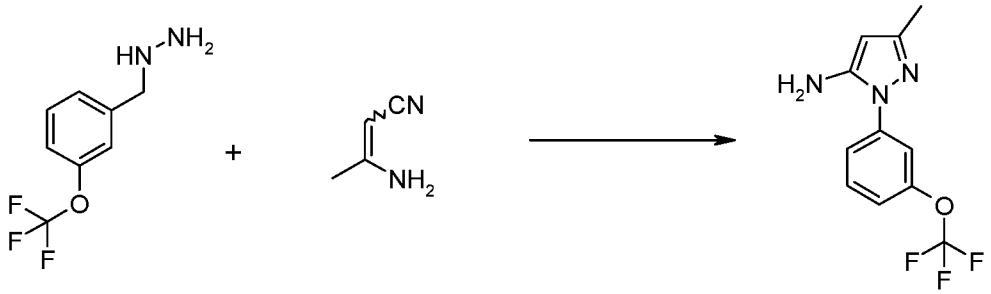
Methods E1-E7: Synthesis of aminopyrazoles

Method E1: Cyclization of hydrazines with 3-aminocrotononitrile



[00342] 3-Aminocrotononitrile (CAS: 1118-61-2, 1.1 equiv), the hydrazine hydrochloride (1.0 equiv) and few drops of 1 N HCl solution are heated in EtOH at reflux until the reaction is finished. The reaction mixture is cooled down to RT and then is diluted with a saturated solution of sodium hydrogencarbonate. The aqueous phase is extracted with dichloromethane. The combined organic phases are filtered through a phase separator and concentrated under vacuum to afford the aminopyrazole which is used as such.

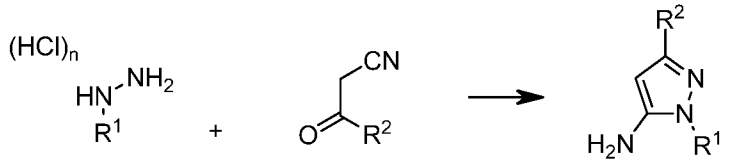
Illustrative synthesis of AMP01: (5-Methyl-2-(3-trifluoromethoxy-phenyl)-2H-pyrazol-3-ylamine



[00343] 3-Aminocrotononitrile (CAS: 1118-61-2, 0.5 g, 6.09 mmol, 1.1 eq;), 3-(trifluoromethoxy)phenylhydrazine hydrochloride (1.27 g, 5.54 mmol, 1.0 equiv) and two drops of 1 N HCl solution were heated in EtOH (1.5 mL) at reflux overnight. The reaction mixture was diluted with a saturated solution of sodium hydrogencarbonate, and the aqueous phase was

extracted with dichloromethane. The combined organic phases were filtered through a phase separator and concentrated under vacuum to afford the titled compound which was used as such.

Method E2: Cyclization of hydrochloride salts of hydrazines with cyano ketones



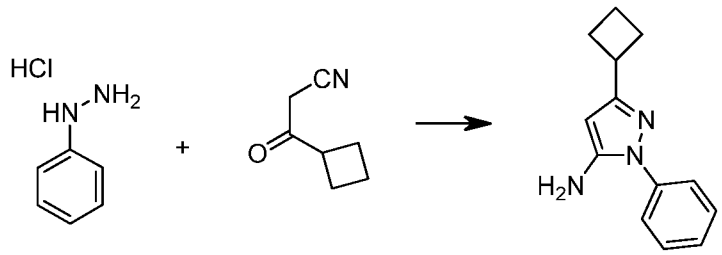
n=1 or 2

[00344] A round bottom flask is charged with the cyanoketone (from 1.0 to 1.5 equiv), the hydrazine hydrochloride or dihydrochloride (1 equiv) and EtOH. This mixture is stirred at a temperature ranging from RT to refluxing ethanol until the reaction is finished. Then the reaction mixture is concentrated in vacuo to afford a crude mixture which is used as such or undergoes one of the following processes:

[00345] Either the crude mixture is taken up in a suitable solvent. The resulting slurry is filtered, and the solids are washed with the same solvent and dried in vacuo to afford the aminopyrazole as its hydrochloride salt which is used as such or is taken up in either ethyl acetate or dichloromethane and basified with a saturated solution of either potassium carbonate or sodium hydrogencarbonate. The two phases are separated, and the aqueous phase is extracted with either ethyl acetate or dichloromethane. The combined organic phases are washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to afford the aminopyrazole as its free base which is used as such or further purified by flash chromatography on silica gel.

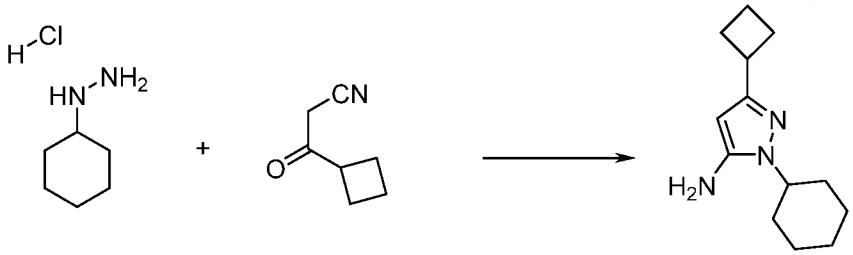
[00346] Or alternatively this crude mixture is partitioned between water and either ethyl acetate or dichloromethane. The two phases are separated, and the aqueous phase is washed with either ethyl acetate or dichloromethane, basified with a saturated solution of sodium hydrogencarbonate and extracted with either ethyl acetate or dichloromethane. The combined organic phases are washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to afford the aminopyrazole as its free base which is used as such or further purified by flash chromatography on silica gel.

Illustrative synthesis of AMP29: 5-Cyclobutyl-2-phenyl-2H-pyrazol-3-ylamine



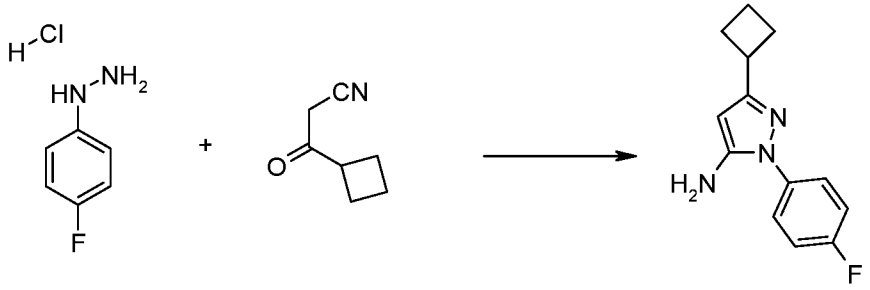
[00347] A round bottom flask was charged with 3-cyclobutyl-3-oxo-propionitrile (CK01, 19.6 g, 159 mmol, 1.1 equiv), phenylhydrazine hydrochloride (CAS: 59-88-1, 20.92 g, 145 mmol, 1.0 equiv) and EtOH (210 mL). The reaction mixture was stirred at reflux for 1 h. Then the reaction mixture was concentrated in vacuo to afford a crude mixture which was taken up in diethyl ether. The resulting slurry was filtered, and the solid was washed with diethyl ether and dried in vacuo to afford the titled compound as its hydrochloride salt which was taken up in dichloromethane and basified with a saturated solution of sodium hydrogencarbonate. The two phases were separated, and the aqueous phase was extracted with dichloromethane. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to afford the titled compound as its free base.

*Illustrative synthesis of AMP 35: 5-Cyclobutyl-2-cyclohexyl-2*H*-pyrazol-3-ylamine*



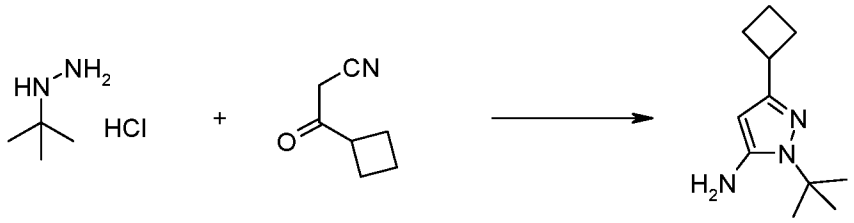
[00348] A round bottom flask was charged with 3-cyclobutyl-3-oxo-propionitrile (CK01, [118431-89-3], 20.4 g, 166 mmol), cyclohexylhydrazine hydrochloride ([24214-73-1], 25 g, 166 mmol) and EtOH (200 mL). The reaction mixture was refluxed overnight and cooled down to RT. Next, the mixture was concentrated and water (150 mL) was added. The pH was modified till pH = 7 with a saturated K_2CO_3 solution. Subsequently, the aqueous phase was extracted with DCM. The obtained organic phase was dried and concentrated to give a yellow solid. Trituration with MTBE gave the titled compound.

Illustrative synthesis of AMP93: 3-cyclobutyl-1-(4-fluorophenyl)-1H-pyrazol-5-amine



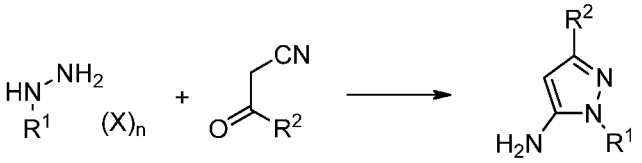
[00349] A round bottom flask was charged with 3-cyclobutyl-3-oxo-propionitrile (CK01, 10 g, 81.4 mmol), 4-fluorophenylhydrazine hydrochloride ([823-85-8], 12 g, 74 mmol) and EtOH (35 mL). The reaction mixture was refluxed for 2 hours and cooled down to RT. Half of the solvent was removed in vacuo. The mixture was vigorously stirred and diisopropyl ether (350 mL) was added. The stirring was continued for 1 hour, and the formed precipitate was filtered, washed with diisopropyl ether and dried at 40 °C under reduced pressure to give the titled compound.

Illustrative synthesis of AMP94: 1-tert-butyl-3-cyclobutyl-1H-pyrazol-5-amine



[00350] A round bottom flask was charged with 3-cyclobutyl-3-oxo-propionitrile (CK01, 12.3 g, 0.1 mol), *tert*-butylhydrazine hydrochloride ([7400-27-3], 13.5 g, 0.11 mol) and EtOH (150 mL). The reaction mixture was refluxed for 20 hours and cooled down to RT. Half of the solvent was removed by concentration in vacuo, and the mixture was cooled in an ice bath. The formed precipitate was collected by filtration and washed successively with diethyl ether and *n*-pentane. The filtrate was allowed to stand for 1 hour, and the formed precipitate was again collected by filtration and washed with diethyl ether and *n*-pentane. The combined solids were stirred in ethyl acetate and a saturated solution of $NaHCO_3$. The organic phase was dried over sodium sulfate, filtered and evaporated under reduced pressure to give the titled compound.

Method E3: Cyclization of cyano ketones with hydrazines either as free base, hydrochloride or TFA salt, in the presence of an organic base

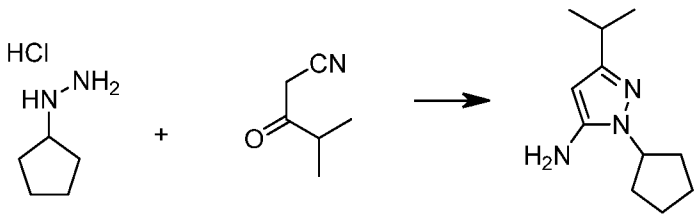


X = HCl or TFA

n= 0, 1, 2

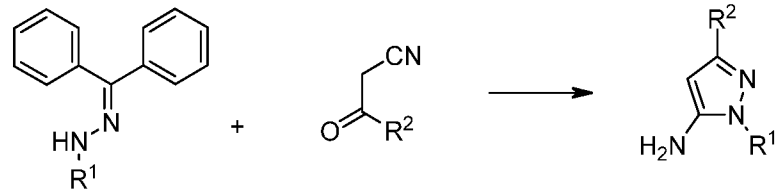
[00351] To the hydrazine either as free base or as a hydrochloride or a trifluoroacetic acid mono or di-salt (1 equiv) and the cyanoketone (from 1.0 to 1.5 equiv) in ethanol or toluene at RT is added DIPEA (from 0 to 2.0 equiv). Then the reaction mixture is heated at reflux until the reaction is finished. The reaction mixture is concentrated in vacuo to afford a crude mixture which is used as such or purified by flash chromatography on silica gel to afford the aminopyrazole as its free base.

Illustrative synthesis of AMP26: 2-Cyclopentyl-5-isopropyl-2H-pyrazol-3-ylamine



[00352] To cyclopentylhydrazine hydrochloride (CAS: 24214-72-0, 0.35 g, 2.56 mmol, 1.0 equiv) and 4-methyl-3-oxo-pentanenitrile (CAS: 29509-06-6, 0.33 mL, 2.82 mmol, 1.1 equiv) in toluene (12.8 mL) at RT was added DIPEA (0.82 mL, 5.12 mmol, 2.0 equiv). Then the reaction mixture was heated at reflux for 1.5 h. The reaction mixture was cooled down to RT and concentrated in vacuo to afford a crude mixture which was purified by flash chromatography on silica gel (eluent system: heptane/ethyl acetate gradient from 100/0 to 30/70) to afford the titled compound.

Method E4: Cyclization of arylhydrazones with cyanoketones

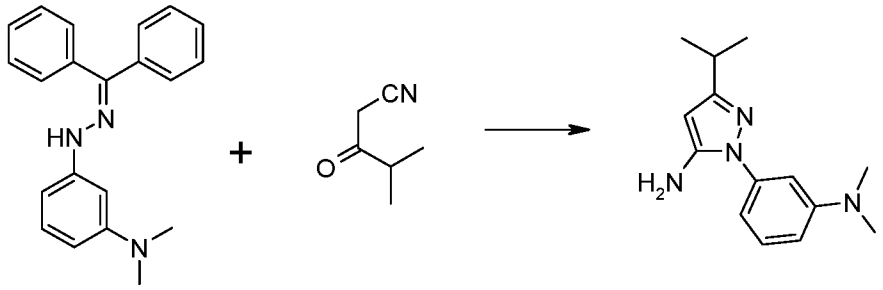


[00353] To the arylhydrazone (1 equiv) and the cyanoketone (from 1.0 to 2 equiv) in ethanol at RT is added an aqueous solution of 2 M HCl or 12 M HCl (5 equiv). Then the reaction mixture is heated at reflux until the reaction is finished. Then the reaction mixture is cooled down to RT and undergoes one of the following processes.

[00354] The reaction mixture is concentrated to dryness in vacuo to afford a crude mixture. The aminopyrazole is obtained from this crude mixture by precipitation from a suitable solvent to afford the aminopyrazole as its hydrochloride salt and used as such.

[00355] Ethanol from the reaction mixture is removed in vacuo. The resulting aqueous residue is diluted with an aqueous solution of 2 M HCl, washed with dichloromethane, then basified with a saturated solution of sodium hydrogencarbonate and extracted with dichloromethane. The combined organic phases are washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to afford the aminopyrazole as a free base which is used as such or further purified by flash chromatography on silica gel.

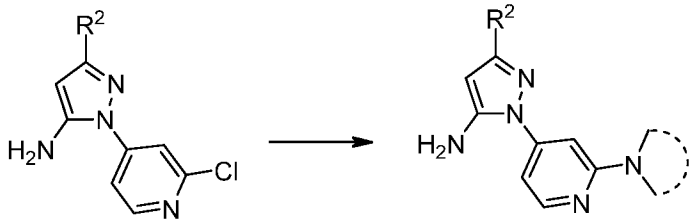
Illustrative synthesis of AMP06: 2-(3-Dimethylamino-phenyl)-5-isopropyl-2H-pyrazol-3-ylamine



[00356] To [3-(*N*'-benzhydrylidene-hydrazino)-phenyl]-dimethyl-amine (ArH01, 25.57g, 81 mmol, 1 equiv) and 4-methyl-3-oxo-pentanenitrile (CAS: 29509-06-6, 10.57 mL, 89.2 mmol, 1.1 equiv) in ethanol (255 mL) at RT was added an aqueous solution of 2 M HCl (203 mL, 405 mmol, 5 equiv). Then the reaction mixture was heated at reflux overnight. The reaction mixture was cooled down to RT, and ethanol from the reaction mixture was removed in vacuo. The

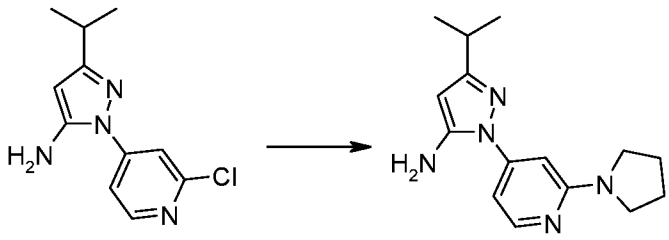
resulting aqueous residue was diluted with an aqueous solution of 2 M HCl, washed with dichloromethane, then basified with a saturated solution of sodium hydrogencarbonate and extracted twice with dichloromethane. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to afford the titled compound which was used as such.

Method E5: SNAr on 2-(2-chloro-pyridin-4-yl)-yl-2H-pyrazol-3-ylamine intermediates



[00357] A sealed tube is charged with the 2-(2-chloro-pyridin-4-yl)-yl-2*H*-pyrazol-3-ylamine intermediate (1 equiv), the amine (from 10 to 15 equiv), DIPEA (3equiv) and DMA. This mixture is heated at a temperature ranging from 130 °C to 160 °C until the reaction is finished. Then the reaction mixture is cooled down to RT and partitioned between ethyl acetate and water. The two phases are separated and the aqueous phase is extracted with ethyl acetate. The combined organic phases are washed with water and brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The substituted aminopyrazole is obtained from the crude mixture either by precipitation or by purification by flash chromatography on silica gel.

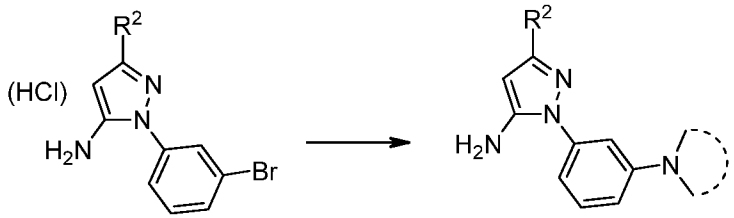
Illustrative synthesis of AMP22: 5-Isopropyl-2-(2-pyrrolidin-1-yl-pyridin-4-yl)-2H-pyrazol-3-ylamine



[00358] A sealed tube was charged with 2-(2-chloro-pyridin-4-yl)-yl-2*H*-pyrazol-3-ylamine intermediate (AMP20, 1.2 g, 5.07 mmol, 1 equiv), pyrrolidine (CAS: 123-75-1, 4 mL, 50.7 mmol, 10 equiv), DIPEA (2.6 mL, 15.2 mmol, 3equiv) and DMA (10 mL). This mixture was heated at 130 °C for 2 h. Then the reaction mixture was cooled down to RT, and additional

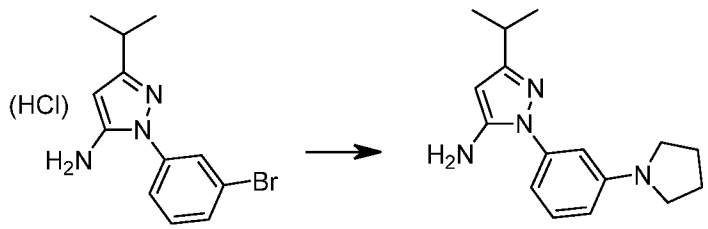
pyrrolidine (CAS: 123-75-1, 1 mL, 12.67 mmol, 2.5 equiv) was introduced, and the reaction mixture was heated at 130 °C for 30 minutes. Then the reaction mixture was cooled down to RT and partitioned between ethyl acetate and water. The two phases were separated, and the aqueous phase was extracted twice with ethyl acetate. The combined organic phases were washed with water (three times) and brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The crude mixture was purified by flash chromatography on silica gel (eluent system: dichloromethane/methanol gradient from 100/0 to 97/3) to afford the titled compound.

Method E6: Buchwald coupling



[00359] To the 2-(3-bromo-phenyl)-2*H*-pyrazol-3-ylamine hydrochloride salt intermediate (1 equiv) in anhydrous THF at RT under a nitrogen atmosphere is added the amine (1.2 equiv), a solution of 1 N LiHMDS in THF (5 equiv) and XPhos Pd G1 (CAS 1028206-56-5, 0.1 equiv). The reaction mixture is stirred at RT until the reaction is finished. The reaction mixture is hydrolyzed with a saturated solution of ammonium chloride and diluted with dichloromethane. The two phases are separated, and the aqueous phase is extracted with dichloromethane. The combined organic phases are washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The substituted aminopyrazole is obtained from the crude mixture by purification with flash chromatography on silica gel (eluent system: heptane/ethyl acetate).

Illustrative synthesis of AMP11: 5-Isopropyl-2-(3-pyrrolidin-1-yl-phenyl)-2H-pyrazol-3-ylamine



[00360] To 2-(3-bromo-phenyl)-5-isopropyl-2*H*-pyrazol-3-ylamine hydrochloride salt (AMP05, 0.5g, 1.58 mmol, 1 equiv) in anhydrous THF (5 mL) at RT under nitrogen atmosphere

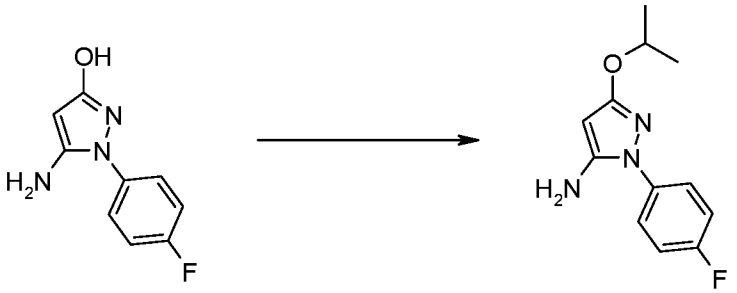
was added pyrrolidine (CAS: 123-75-1, 0.16 mL, 1.9 mmol, 1.2 equiv), a solution of 1 N LiHMDS in THF (8mL, 8 mmol, 5 equiv) and XPhos Pd G1 (CAS 1028206-56-5, 0.117 g, 0.16 mmol, 0.1 equiv). The reaction mixture was stirred at RT for 5 h. The reaction mixture was treated with a saturated solution of ammonium chloride and diluted with dichloromethane. The two phases were separated, and the aqueous phase was extracted with dichloromethane. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The crude mixture was purified by flash chromatography on silica gel (eluent system: heptane/ethyl acetate gradient from 100/0 to 65/35) to afford the titled compound.

Method E7: O-Alkylation of 5-aminopyrazol-3-ol analogues



[00361] A suspension of 5-aminopyrazol-3-ol derivative (1 equiv), cesium carbonate (1.2 equiv) and 2-bromopropane (1 equiv) in *N*-methylpyrrolidine is stirred at RT for 20 to 72 hours. The reaction mixture is diluted with DCM and washed with water. The organic phase is dried over sodium sulfate, filtered and concentrated under reduced pressure. The *O*-alkylated product is purified by flash column chromatography on silica gel.

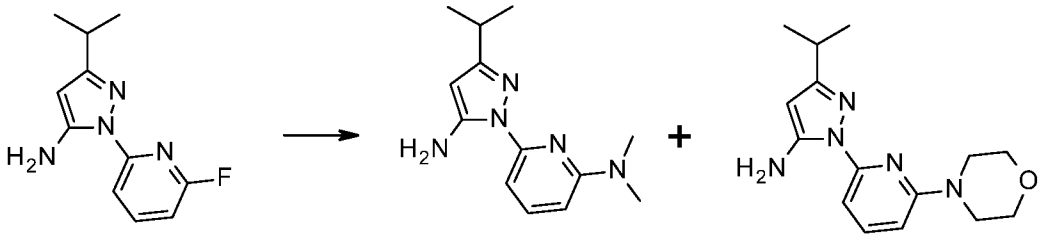
Illustrative synthesis of AMP96: 1-(4-fluorophenyl)-3-[(propan-2-yl)oxy]-1H-pyrazol-5-amine



[00362] A suspension of 5-amino-1-(4-fluorophenyl)-1*H*-pyrazol-3-ol ([1247169-18-1], 800 mg, 4.14 mmol), cesium carbonate (2.15 g, 4.97 mmol) and 2-bromopropane (516 µL, 4.14 mmol) in *N*-methylpyrrolidine (8 mL) was stirred at RT for 20 hours. The reaction mixture was diluted with DCM and washed with water. The organic phase was dried over sodium sulfate,

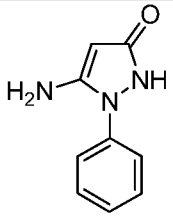
filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel eluting with ethyl acetate/*n*-heptane to yield the titled compound.

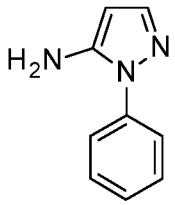
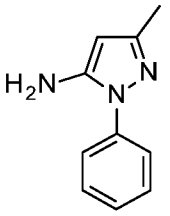
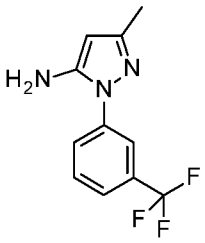
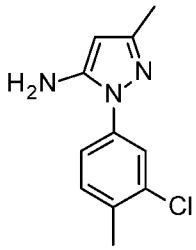
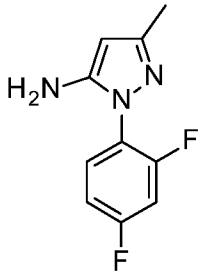
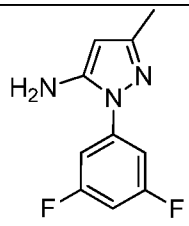
Synthesis of intermediates AMP18 and AMP19: [6-(5-Amino-3-isopropyl-pyrazol-1-yl)-pyridin-2-yl]-dimethyl-amine and 5-Isopropyl-2-(6-morpholin-4-yl-pyridin-2-yl)-2H-pyrazol-3-ylamine

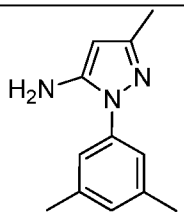
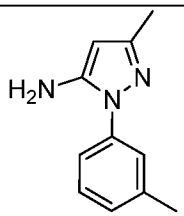
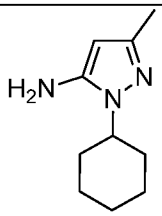
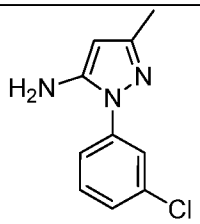
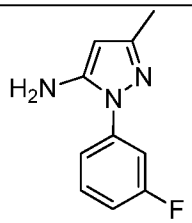
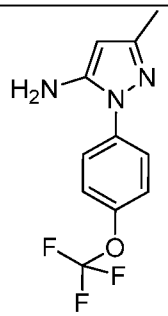


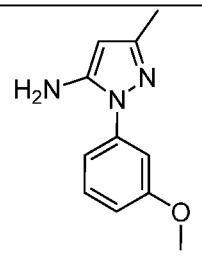
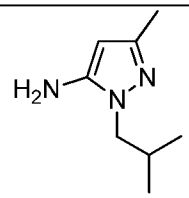
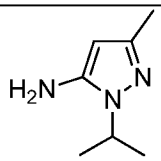
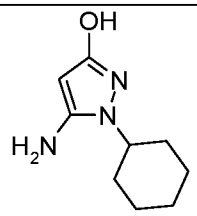
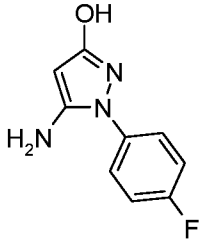
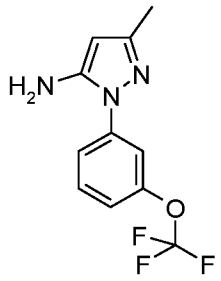
[00363] A sealed tube was charged with 2-(6-fluoro-pyridin-2-yl)-5-isopropyl-2H-pyrazol-3-ylamine (AMP17, 0.2 g, 0.91 mmol, 1 equiv), morpholine (CAS: 110-91-8, 0.12 mL, 1.37 mmol, 1.5 equiv), DIPEA (0.19 mL, 1.09 mmol, 1.2 equiv) and DMF (2 mL). This mixture was heated at 100 °C overnight. Then the reaction mixture was cooled down to RT and partitioned between ethyl acetate and water. The two phases were separated, and the aqueous phase was extracted with ethyl acetate. The combined organic phases were washed with water (three times) and brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The crude mixture was purified by flash chromatography on silica gel (eluent system: heptane/ethyl acetate gradient from 100/0 to 60/40) to afford the two titled compounds.

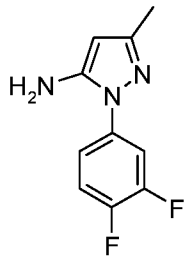
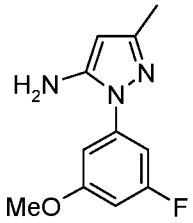
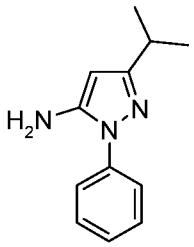
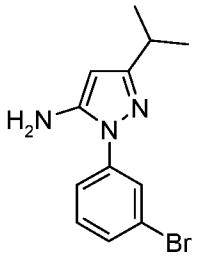
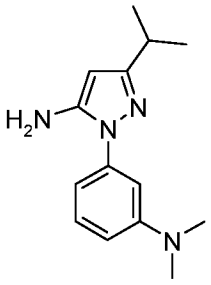
Table V. List of aminopyrazoles

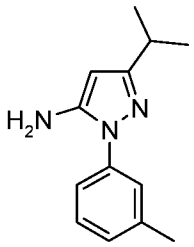
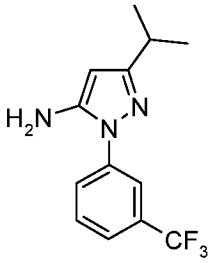
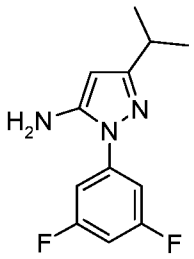
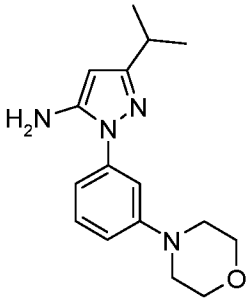
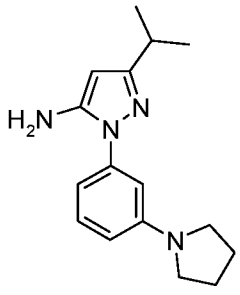
Int.	Structure	Name	SM	method	MW	Mes
70373-98-7		5-Amino-1-phenyl-1,2-dihydro-pyrazol-3-one			175	

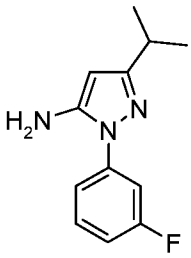
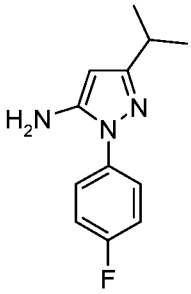
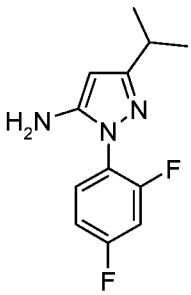
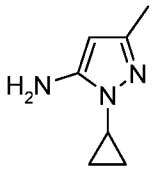
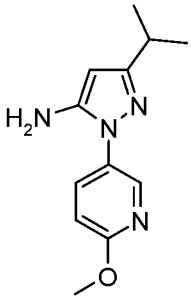
Int.	Structure	Name	SM	method	MW	Mes
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1131-18-6		5-Methyl-2-phenyl-2*H*-pyrazol-3-ylamine			173	
345-07-3		5-Methyl-2-(3-trifluoromethyl-phenyl)-2*H*-pyrazol-3-ylamine			241	
866472-29-9		2-(3-Chloro-4-methyl-phenyl)-5-methyl-2*H*-pyrazol-3-ylamine			221	
380569-79-9		2-(2,4-Difluoro-phenyl)-5-methyl-2*H*-pyrazol-3-ylamine			209	
1232796-65-4		2-(3,5-Difluoro-phenyl)-5-methyl-2*H*-pyrazol-3-ylamine			209	

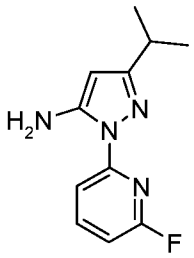
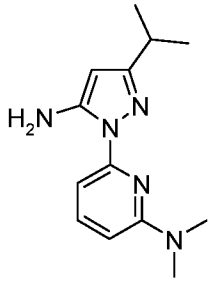
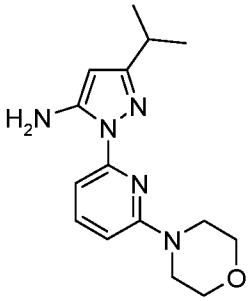
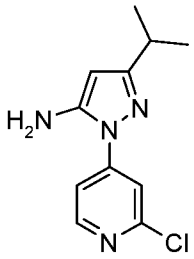
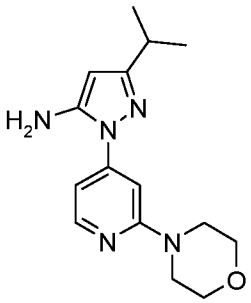
Int.	Structure	Name	SM	method	MW	Mes
890010-89-6		2-(3,5-Dimethyl-phenyl)-5-methyl-2*H*-pyrazol-3-ylamine			201	
92721-83-0		5-Methyl-2-*m*-tolyl-2*H*-pyrazol-3-ylamine			187	
56547-82-1		2-Cyclohexyl-5-methyl-2*H*-pyrazol-3-ylamine			179	
40401-41-0		2-(3-Chloro-phenyl)-5-methyl-2*H*-pyrazol-3-ylamine			207	
105438-45-7		2-(3-Fluoro-phenyl)-5-methyl-2*H*-pyrazol-3-ylamine			191	
497141-59-0		5-Methyl-2-(4-trifluoromethoxy-phenyl)-2*H*-pyrazol-3-ylamine			257	

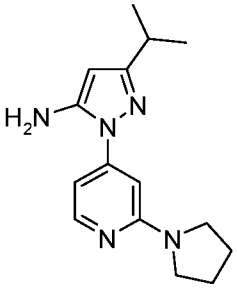
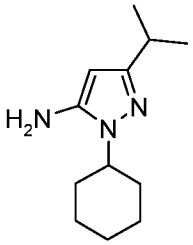
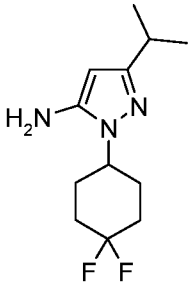
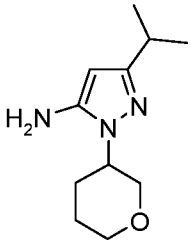
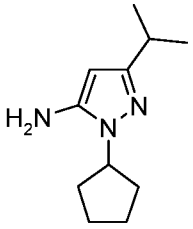
Int.	Structure	Name	SM	method	MW	Mes
92721-94-3		2-(3-Methoxy-phenyl)-5-methyl-2*H*-pyrazol-3-ylamine			203	
3524-36-5		2-Isobutyl-5-methyl-2*H*-pyrazol-3-ylamine			153	
1124-16-9		2-Isopropyl-5-methyl-2*H*-pyrazol-3-yL amine			139	
436088-86-7		5-Amino-1-cyclohexyl-1*H*-pyrazol-3-ol			181	
1247169-18-1		5-Amino-1-(4-fluorophenyl)-1*H*-pyrazol-3-ol			193	
AMP01		5-Methyl-2-(3-trifluoromethoxy-phenyl)-2*H*-pyrazol-3-ylamine	133115-55-6, 1118-61-2	E1 Specific example	257	258

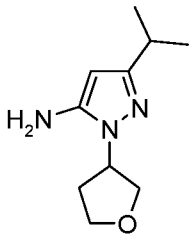
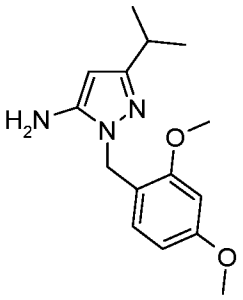
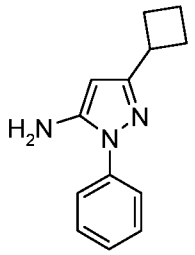
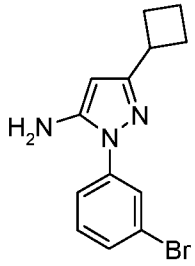
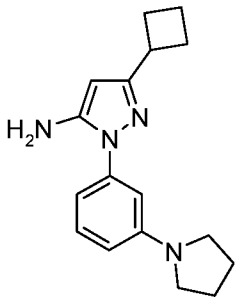
Int.	Structure	Name	SM	method	MW	Mes
AMP02		2-(3,4-Difluoro-phenyl)-5-methyl-2*H*-pyrazol-3-ylamine	161886-22-2, 1118-22-2	E1	209	210
AMP03		2-(3-Fluoro-5-methoxy-phenyl)-5-methyl-2*H*-pyrazol-3-ylamine	ArH03, 1118-61-2	E4	221	222
AMP04		5-Isopropyl-2-phenyl-2*H*-pyrazol-3-ylamine	100-63-0, 29509-06-6	E3	201	202
AMP05		2-(3-Bromo-phenyl)-5-isopropyl-2*H*-pyrazol-3-ylamine	27246-81-7, 29509-06-6	E2	280	281
AMP06		2-(3-Dimethylamino-phenyl)-5-isopropyl-2*H*-pyrazol-3-ylamine	ArH01, 29509-06-6	E4 Specific example	244	245

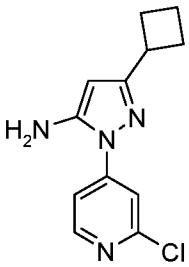
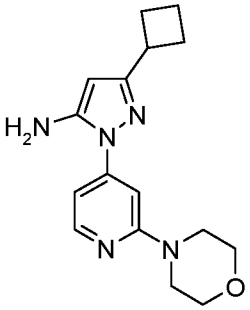
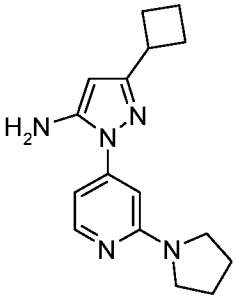
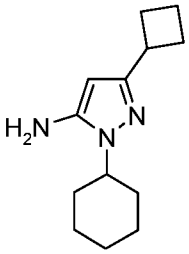
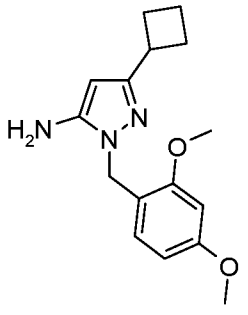
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AMP07		5-Isopropyl-2-*m*-tolyl-2*H*-pyrazol-3-ylamine	637-04-7, 29509-06-6	E2	215	216
AMP08		5-Isopropyl-2-(3-trifluoromethyl-phenyl)-2*H*-pyrazol-3-ylamine	368-78-5, 29509-06-6	E3	269	270
AMP09		2-(3,5-Difluoro-phenyl)-5-isopropyl-2*H*-pyrazol-3-ylamine	134993-88-7, 29509-06-6	E2	237	238
AMP10		5-Isopropyl-2-(3-morpholin-4-yl-phenyl)-2*H*-pyrazol-3-ylamine	ArH02, 29509-06-6	E4	286	287
AMP11		5-Isopropyl-2-(3-pyrrolidin-1-yl-phenyl)-2*H*-pyrazol-3-ylamine	AMP05	E6 Specific example	270	271

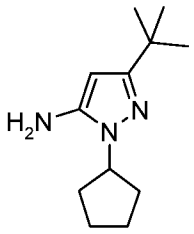
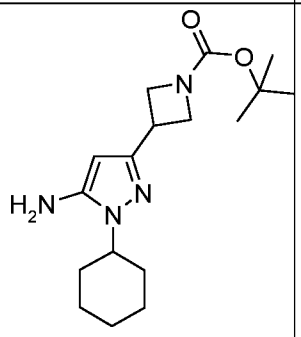
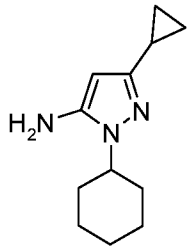
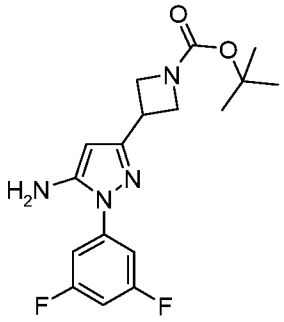
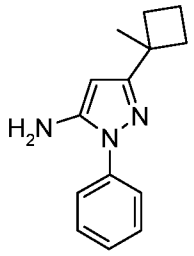
Int.	Structure	Name	SM	method	MW	Mes
AMP12		2-(3-Fluoro-phenyl)-5-isopropyl-2*H*-pyrazol-3-ylamine	502496-27-7, 2950906-6	E2	219	220
AMP13		2-(4-Fluoro-phenyl)-5-isopropyl-2*H*-pyrazol-3-ylamine	823-85-8, 29509-06-6	E2	219	220
AMP14		2-(2,4-Difluoro-phenyl)-5-isopropyl-2*H*-pyrazol-3-ylamine	51523-79-6, 29509-06-6	E2	237	238
AMP15		2-Cyclopropyl-5-methyl-2*H*-pyrazol-3-ylamine	213764-25-1, 1118-61-2	E1	137	138
AMP16		5-Isopropyl-2-(6-methoxy-pyridin-3-yl)-2*H*-pyrazol-3-ylamine	179543-88-5, 29509-06-6	E2	232	233

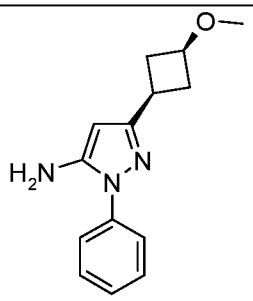
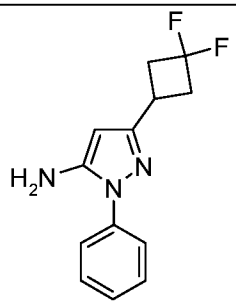
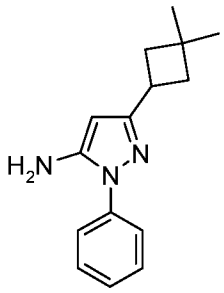
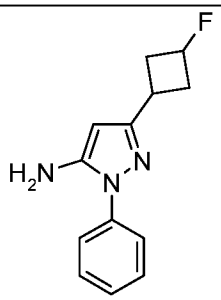
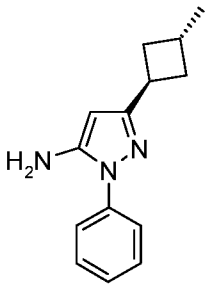
Int.	Structure	Name	SM	method	MW	Mes
AMP17		2-(6-Fluoro-pyridin-2-yl)-5-isopropyl-2*H*-pyrazol-3-ylamine	ArH04, 29509-06-6	E4	220	221
AMP18		[6-(5-Amino-3-isopropyl-pyrazol-1-yl)-pyridin-2-yl]-dimethyl-amine	AMP17	Specific example	245	246
AMP19		5-Isopropyl-2-(6-morpholin-4-yl-pyridin-2-yl)-2*H*-pyrazol-3-ylamine	AMP17	Specific example	287	288
AMP20		2-(2-Chloro-pyridin-4-yl)-5-isopropyl-2*H*-pyrazol-3-ylamine	ArH05, 29509-06-6	E4	237	238
AMP21		5-Isopropyl-2-(2-morpholin-4-yl-pyridin-4-yl)-2*H*-pyrazol-3-ylamine	AMP20	E5	287	288

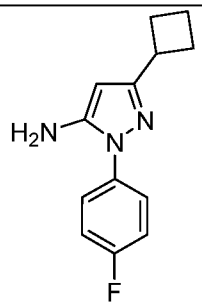
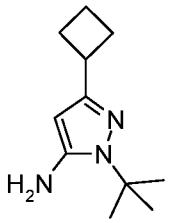
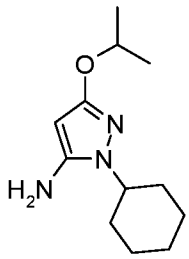
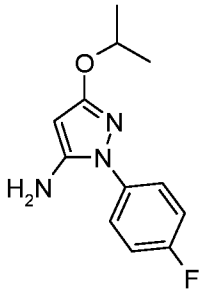
Int.	Structure	Name	SM	method	MW	Mes
AMP22		5-Isopropyl-2-(2-pyrrolidin-1-yl-pyridin-4-yl)-2*H*-pyrazol-3-ylamine	AMP20	E5 Specific example	271	272
AMP23		2-Cyclohexyl-5-isopropyl-2*H*-pyrazol-3-ylamine	30929-57-8, 29509-06-6	E2	207	208
AMP24		2-(4,4-Difluoro-cyclohexyl)-5-isopropyl-2*H*-pyrazol-3-ylamine	H02, 29509-06-6	E3	243	244
AMP25		5-Isopropyl-2-(tetrahydro-pyran-3-yl)-2*H*-pyrazol-3-ylamine	H01, 29509-06-6	E3	209	210
AMP26		2-Cyclopentyl-5-isopropyl-2*H*-pyrazol-3-ylamine	24214-72-0, 29509-06-6	E3 Specific example	193	194

Int.	Structure	Name	SM	method	MW	Mes
AMP27		5-Isopropyl-2-(tetrahydro-furan-3-yl)-2*H*-pyrazol-3-ylamine	H03, 29509-06-6	E3	195	196
AMP28		2-(2,4-Dimethoxy-benzyl)-5-isopropyl-2*H*-pyrazol-3-ylamine	H04, 29509-06-6	E2	275	276
AMP29		5-Cyclobutyl-2-phenyl-2*H*-pyrazol-3-ylamine	59-88-1, CK01	E2 Specific example	213	214
AMP30		2-(3-Bromo-phenyl)-5-cyclobutyl-2*H*-pyrazol-3-ylamine	27246-81-7, CK01	E3	292	293
AMP31		5-Cyclobutyl-2-(3-pyrrolidin-1-yl-phenyl)-2*H*-pyrazol-3-ylamine	AMP30	E6	282	283

Int.	Structure	Name	SM	method	MW	Mes
AMP32		2-(2-Chloro-pyridin-4-yl)-5-cyclobutyl-2*H*-pyrazol-3-ylamine	700811-29-6, CK01	E3	248	249
AMP33		5-Cyclobutyl-2-(2-morpholin-4-yl-pyridin-4-yl)-2*H*-pyrazol-3-ylamine	AMP32	E5	299	300
AMP34		5-Cyclobutyl-2-(2-pyrrolidin-1-yl-pyridin-4-yl)-2*H*-pyrazol-3-ylamine	AMP32	E5	283	284
AMP35		5-Cyclobutyl-2-cyclohexyl-2*H*-pyrazol-3-ylamine	30929-57-8, CK01	E2, Specific Example	219	220
AMP36		5-Cyclobutyl-2-(2,4-dimethoxy-benzyl)-2*H*-pyrazol-3-ylamine	H04, CK01	E2	287	288

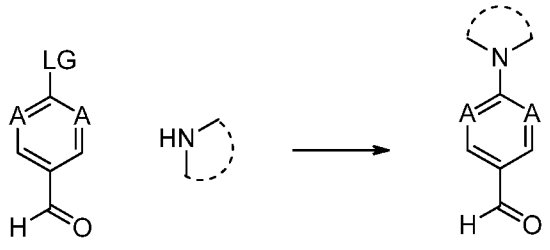
Int.	Structure	Name	SM	method	MW	Mes
AMP37		5-*tert*-Butyl-2-cyclopentyl-2*H*-pyrazol-3-ylamine	24214-72-0, 599917-51-2	E2	207	208
AMP38		3-(5-Amino-1-cyclohexyl-1*H*-pyrazol-3-yl)-azetidine-1-carboxylic acid *tert*-butyl ester	30929-57-8, 887594-13-0	E2	320	321
AMP39		2-Cyclohexyl-5-cyclopropyl-2*H*-pyrazol-3-ylamine	30929-57-8, 118431-88-2	E2	205	206
AMP40		3-[5-Amino-1-(3,5-difluoro-phenyl)-1*H*-pyrazol-3-yl]-azetidine-1-carboxylic acid *tert*-butyl ester	134993-88-7, 887594-13-0	E2	350	295[1]
AMP41		5-(1-Methyl-cyclobutyl)-2-phenyl-2*H*-pyrazol-3-ylamine	100-63-0, CK02	E3	227	228

Int.	Structure	Name	SM	method	MW	Mes
AMP42		5-(3-Methoxy-cyclobutyl)-2-phenyl-2*H*-pyrazol-3-ylamine	59-88-1, CK03	E2	243	
AMP43		5-(3,3-Difluoro-cyclobutyl)-2-phenyl-2*H*-pyrazol-3-ylamine	59-88-1, 1234616-26-2	E2	249	
AMP44		5-(3,3-Dimethyl-cyclobutyl)-2-phenyl-2*H*-pyrazol-3-ylamine	59-88-1, CK04	E2	241	
AMP45		5-(3-Fluoro-cyclobutyl)-2-phenyl-2*H*-pyrazol-3-ylamine	59-88-1, CK05	E2	231	
AMP46		5-(*trans*-3-Methyl-cyclobutyl)-2-phenyl-2*H*-pyrazol-3-ylamine	59-88-1, CK06	E2	227.31	

Int.	Structure	Name	SM	method	MW	Mes
AMP93		3-Cyclobutyl-1-(4-fluorophenyl)-1*H*-pyrazol-5-amine	823-85-8, CK01	Specific example	231	232
AMP94		1-*tert*-Butyl-3-cyclobutyl-1*H*-pyrazol-5-amine	7400-27-3, 118431-89-3	Specific example	193	194
AMP95		1-Cyclohexyl-3-[(propan-2-yl)oxy]-1*H*-pyrazol-5-amine	436088-86-7	E7	223	224
AMP96		1-(4-Fluorophenyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazol-5-amine	1247169-18-1	E7, Specific example	235	236

[1] $(M\text{-}tBu+H)^+$

Method F: Synthesis of aldehydes by SN-Ar

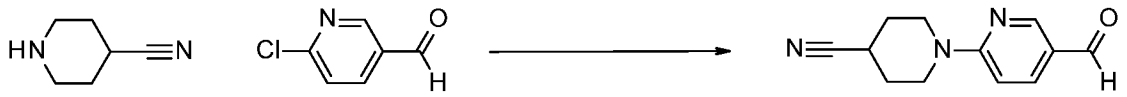


A is either CH or N

LG is F, Cl, or Br

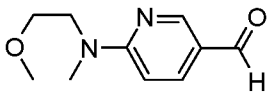
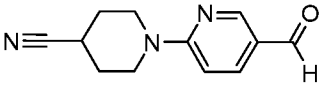
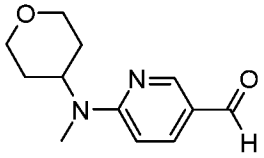
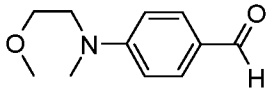
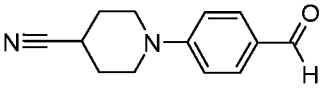
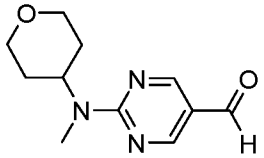
[00364] A solution of the aldehyde (1 equiv), the amine (1.3 to 2 equiv) and the base (DIPEA or K_2CO_3) (2 equiv) is prepared in acetonitrile, DMSO or DMA. This mixture is heated under thermal conditions or under microwave irradiations at a temperature ranging from 85 °C to 150 °C. The reaction is worked up either by filtration of the base when needed or by diluting the reaction mixture with ethyl acetate or DCM and washing the organic phase with water and brine. In all cases, the organic phase is concentrated under reduced pressure, and the crude residue is used as such or purified either by flash column chromatography or precipitation to give the titled compound.

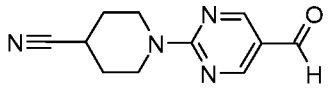
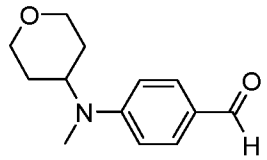
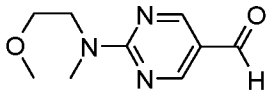
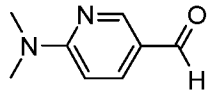
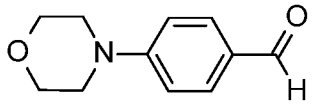
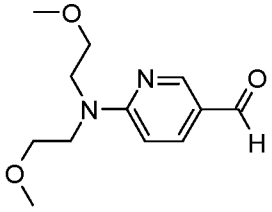
Illustrative synthesis of ALD02: 5'-Formyl-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-carbonitrile



[00365] A solution of 2-chloropyridine-5-carboxaldehyde (CAS: 23100-12-1, 25.1 g, 177.4 mmol), 4-cyanopiperidine (CAS: 4395-98-6, 25.4 g, 230.6 mmol) and DIPEA (62 mL, 354.7 mmol) in acetonitrile (250 mL) was refluxed for 20 hours. The reaction mixture was cooled to RT, and the mixture was concentrated under reduced pressure. The residue was dissolved in DCM (500 mL) and washed successively with a saturated aqueous solution of Na_2CO_3 (250 mL) and brine (250 mL). The organic phase was stirred for 2 minutes with 10 g of silica gel, dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting mixture was dissolved in DCM (150 mL) and poured into a stirring solution of diisopropyl ether (1.5 L). The mixture was stirred vigorously for 4 hours. The precipitate was collected by filtration, washed with diisopropyl ether, and dried at 40 °C under reduced pressure to give the titled compound.

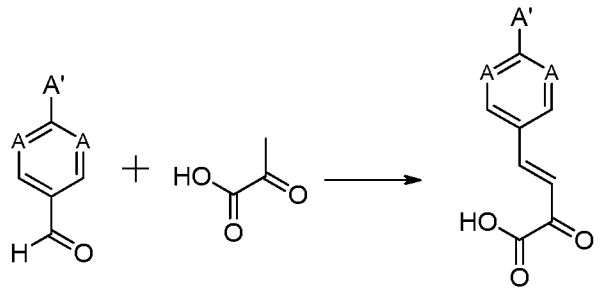
Table VI. List of aldehydes

Int.	Structure	Name	SM	method	MW	Mes
ALD01		6-[(2-Methoxy-ethyl)-methyl-amino]-pyridine-3-carbaldehyde	23100-12-1	F	194	195
ALD02		5'-Formyl-3,4,5,6-tetrahydro-2*H*-[1,2']bipyridinyl-4-carbonitrile	23100-12-1	F, Specific example	215	216
ALD03		6-[Methyl-(tetrahydro-pyran-4-yl)-amino]-pyridine-3-carbaldehyde	23100-12-1	F	220	221
ALD04		4-[(2-Methoxy-ethyl)-methyl-amino]-benzaldehyde	459-57-4	F	193	194
ALD05		1-(4-Formyl-phenyl)-piperidine-4-carbonitrile	459-57-4	F	214	215
ALD06		2-[Methyl-(tetrahydro-pyran-4-yl)-amino]-pyrimidine-5-carbaldehyde	933702-55-7	F	221	222

Int.	Structure	Name	SM	method	MW	Mes
ALD07		1-(5-Formyl-pyrimidin-2-yl)-piperidine-4-carbonitrile	933702-55-7	F	216	217
ALD08		4-[Methyl-(tetrahydro-pyran-4-yl)-amino]-benzaldehyde	459-57-4	F	219	220
ALD09		2-[(2-Methoxy-ethyl)-methyl-amino]-pyrimidine-5-carbaldehyde	933702-55-7	F	195	196
ALD10		6-Dimethylamino-pyridine-3-carbaldehyde	23100-12-1	F	150	151
ALD11 1204-86-0		4-Morpholinobenzaldehyde			191	
ALD12		6-[bis(2-methoxyethyl)amino]pyridine-3-carbaldehyde	23100-12-1	F	238	239

Methods G1-G3: Synthesis of alkylidene pyruvate

Method G1: Synthesis of alkylidene pyruvate



A is either N or CH

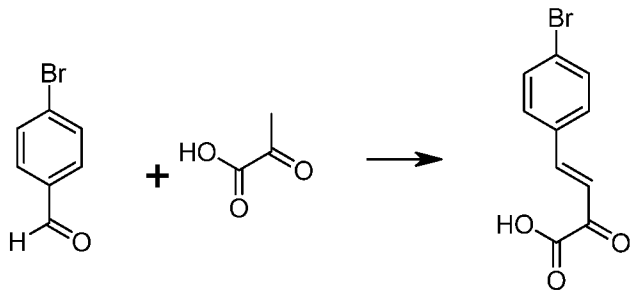
A' is either R^e or L^1-G^{3C} as described in the Summary

[00366] A solution of potassium hydroxide (from1.5 to 2 equiv) in water is added dropwise at 0 °C to a solution of aldehyde (1equiv) and pyruvic acid (CAS 127-17-3, from1 eq to 1.5 equiv) in methanol. The reaction is warmed up to RT and then heated at 40 °C for 1 h to several days. Then the reaction mixture undergoes one of the following processes:

[00367] -Either the formed precipitate is collected by filtration, suspended in an aqueous acidic solution, collected by filtration again, and dried in vacuo to give the titled compound.

[00368] -Or alternatively, methanol is removed in vacuo, and the resulting suspension is filtered. The solid is taken up in water and either ethyl acetate or dichloromethane and acidified to pH=3-5 with either acetic acid or an aqueous solution of 2 M HCl. The two phases are separated, and the aqueous phase is extracted with either ethyl acetate or dichloromethane. The combined organic phases are washed with water and brine, dried over $MgSO_4$, filtered and concentrated in vacuo to afford the titled compound which is used as such or further purified by precipitation.

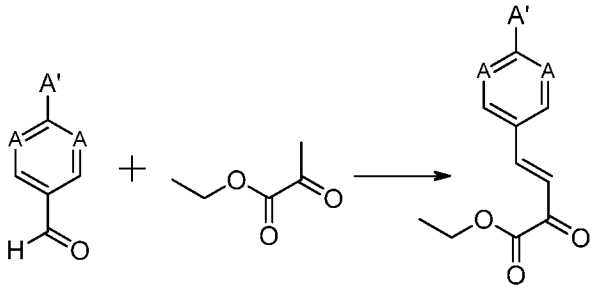
Illustrative synthesis of ALP19: (E)-4-(4-Bromo-phenyl)-2-oxo-but-3-enoic acid



[00369] A solution of potassium hydroxide (6.9 g, 121.6 mmol) in water (45 mL) was added at 0 °C to a stirring solution of 4-bromobenzaldehyde (CAS 1122-91-4, 15 g, 81.1 mmol) and

pyruvic acid (CAS 127-17-3, 5.7 mL, 81.1 mmol) in methanol (105 mL) over a 5 minutes period. The reaction mixture was then heated at 40 °C for 4 hours, cooled down to RT and poured into ice/water (300 mL). The precipitate was stirred for 10 minutes, collected by filtration, washed with water and *n*-heptane, and air dried for 1 hour. The solid was suspended in aqueous 2 N HCl and stirred for 10 minutes. The precipitate was collected by filtration and dried at 40 °C under reduced pressure to afford the titled compound.

Method G2: Synthesis of alkylidene pyruvate

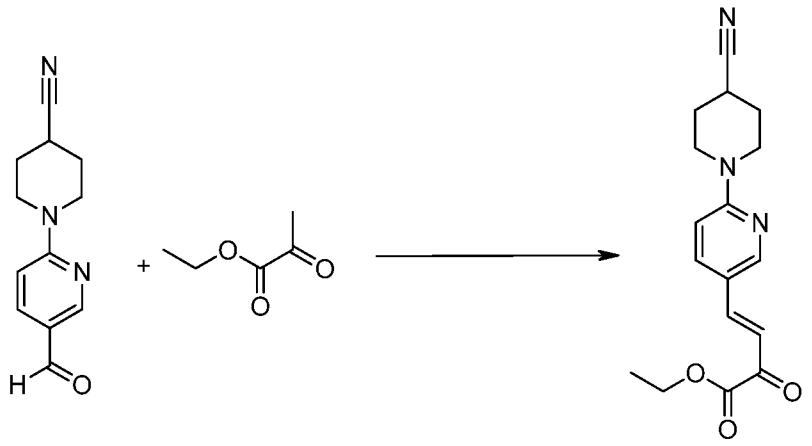


A is either N or CH

A' is either R^e or L^1-G^{3C} as described in the Summary

[00370] Triflic acid (CAS 1493-13-6, from 1.35 eq to 2.5 equiv) is added dropwise to a solution of aldehyde (1 equiv), triethyl orthoformate (CAS 122-51-0, from 1.1 eq to 1.3 equiv) and ethyl pyruvate (CAS 617-35-6, from 1.5 to 3.5 equiv) in chloroform. The solution is refluxed for 30 minutes to 24 h. The reaction mixture is cooled down to RT, diluted with dichloromethane, basified with a saturated aqueous solution of Na_2CO_3 or $NaHCO_3$. The two phases are separated, and the aqueous phase is extracted with dichloromethane. The combined organic phases are dried over sodium sulfate, filtered and concentrated under reduced pressure. This crude mixture is purified either by flash chromatography on silica gel or by precipitation to afford the titled compound.

Illustrative synthesis of ALP09: ethyl (E)-4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-2-oxo-but-3-enoate



[00371] Triflic acid (CAS 1493-13-6, 26.7 mL, 301 mmol) was added dropwise to a solution of intermediate ALD02 (32.4 g, 150.5 mmol), triethyl orthoformate (CAS 122-51-0,32.6 g, 195.7 mmol) and ethyl pyruvate (CAS 617-35-6, 41.7 mL, 376.3 mmol) in chloroform (180 mL). The solution was refluxed for 30 minutes and then cooled to RT. The reaction mixture was diluted with DCM (500 mL) and washed successively with a saturated aqueous solution of Na_2CO_3 (400 mL) and brine (400 mL). The organic phase was dried over sodium sulfate, filtered and concentrated under reduced pressure. The crude sample was purified by flash column chromatography on silica gel eluting with a gradient of *n*-heptane/ethyl acetate to yield the titled compound.

Method G3: Synthesis of alkylidene pyruvate



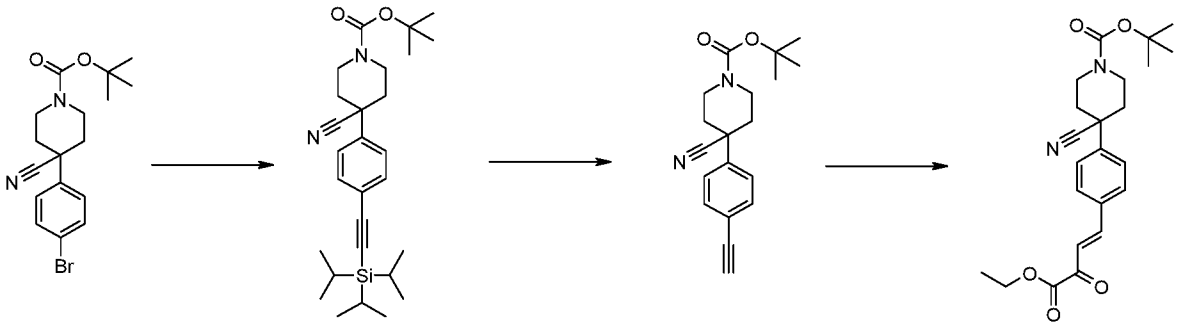
[00372] In a round bottom flask, under a nitrogen atmosphere, a suspension of 4-ethynylbenzene derivative (1 equiv.), 50% ethyl glyoxalate in toluene (2 equiv), morpholine ([110-91-8], 2 equiv), copper(I) bromide ([7787-70-4], 0.5 equiv) in dioxane is heated to 85 °C for 3 to 20 hours. The reaction mixture is cooled to RT, and the solvent was evaporated under reduced pressure. The residue is suspended in a mixture of DCM or DCM/2-propanol (95/5) and is washed twice with water. The organic phase is dried over sodium sulfate, filtered and concentrated under reduced pressure. The crude sample is purified by flash chromatography eluting with ethyl acetate/*n*-heptane/DCM.

Illustrative synthesis of ALP36: ethyl 4-(4-formylphenyl)-2-oxobut-3-enoate



[00373] In a round bottom flask, under a nitrogen atmosphere, a suspension of 4-ethynylbenzaldehyde ([63697-96-1], 5 g, 38.4 mmol), 50% ethyl glyoxalate in toluene ([924-44-7], 15.7 mL, 15.7 g, 76.8 mmol), morpholine ([110-91-8], 6.7 mL, 76.8 mmol), copper(I) bromide ([7787-70-4], 2.8 g, 19.2 mmol) in dioxane (50 mL) was heated to 85 °C for 3 hours. The reaction mixture was cooled to RT, and the volatiles were removed under reduced pressure. The residue was suspended in a mixture of DCM/2-propanol (200 mL, 95/5) and washed twice with water (50 mL). The organic phase was dried over sodium sulfate, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with ethyl acetate/*n*-heptane to yield the titled compound.

Synthesis of ALP38: 4-Cyano-4-[4-((E)-3-ethoxycarbonyl-3-oxo-propenyl)-phenyl]-piperidine-1-carboxylic acid tert-butyl ester



[00374] *Step 1: 4-Cyano-4-{4-[(triisopropylsilanyl)-ethynyl]-phenyl}-piperidine-1-carboxylic acid tert-butyl ester*

[00375] Nitrogen was bubbled for 5 minutes through a suspension of *tert*-butyl 4-(4-bromophenyl)-4-cyanopiperidine-1-carboxylate ([847615-14-9], 547 mg, 1.5 mmol), tetrakis(triphenylphosphine)palladium(0) ([14221-01-3], 90 mg, 77 µmol), copper(I) iodide ([7681-65-4], 8 mg, 42 µmol), lithium chloride ([7447-41-8], 8 mg, 189 µmol), and (triisopropylsilyl)acetylene ([89343-06-6], 670 µL, 3 mmol) in triethylamine (8 mL). The tube was sealed and heated at 100 °C for 6 hours. The mixture was then concentrated under reduced

pressure, and the residue was partitioned between ethyl acetate and water. The organic phase was dried over sodium sulfate, filtered and concentrated in vacuo. The residue was purified by flash column chromatography eluting with ethyl acetate/*n*-heptane to give the titled compound.

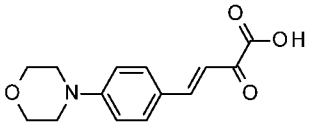
[00376] *Step 2: 4-Cyano-4-(4-ethynyl-phenyl)-piperidine-1-carboxylic acid tert-butyl ester*

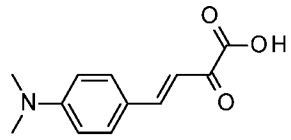
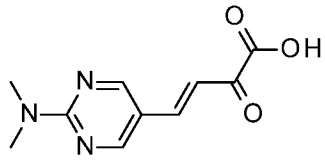
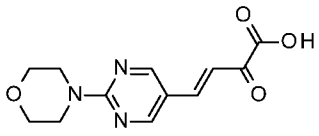
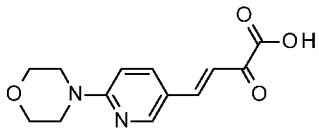
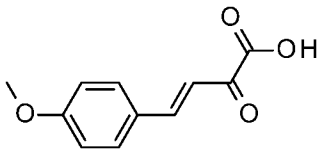
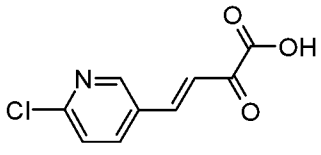
[00377] The compound from Step 1 (700 mg, 1.5 mmol) was dissolved in anhydrous THF (10 mL) and 1 M tetra-*n*-butylammonium fluoride in THF (1.7 mL, 1.7 mmol) was added. The reaction mixture was stirred at RT for 2 hours and then concentrated under reduced pressure. The residue was partitioned between ethyl acetate and water. The organic phase was dried over sodium sulfate, filtered and concentrated in vacuo. The residue was purified by flash column chromatography eluting with ethyl acetate/*n*-heptane to give the titled compound.

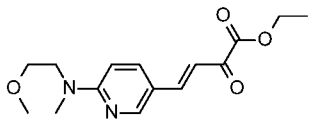
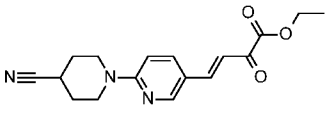
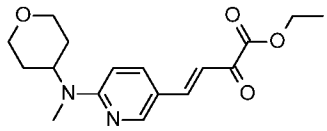
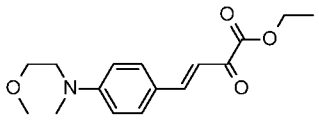
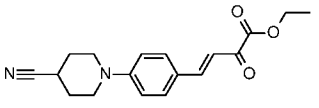
[00378] *Step 3: 4-Cyano-4-[4-((E)-3-ethoxycarbonyl-3-oxo-propenyl)-phenyl]-piperidine-1-carboxylic acid tert-butyl ester*

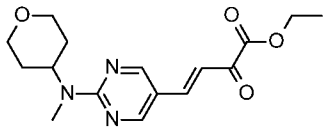
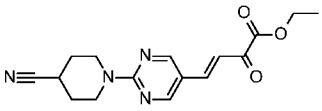
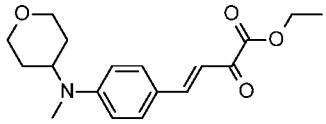
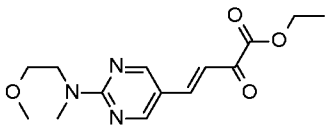
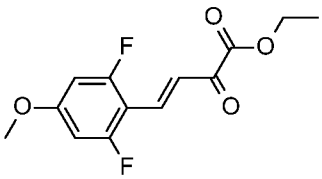
[00379] In a round bottom flask, under a nitrogen atmosphere, a suspension of the compound from Step 2 (270 mg, 0.58 mmol), 50% ethyl glyoxalate in toluene ([924-44-7], 232 µL, 1.16 mmol), morpholine ([110-91-8], 101 µL, 1.16 mmol), and copper(I) bromide ([7787-70-4], 42 mg, 0.29 mmol) in dioxane (5 mL) was heated to 85 °C for 20 hours. The reaction mixture was cooled down to RT and 50% ethyl glyoxalate in toluene ([924-44-7], 232 µL, 1.16 mmol), morpholine ([110-91-8], 101 µL, 1.16 mmol), and copper(I) bromide ([7787-70-4], 42 mg, 0.29 mmol) were added again, and the sealed tube was heated at 100 °C for 1 hour. The reaction mixture was cooled to RT and concentrated under reduced pressure. The residue was suspended in DCM (20 mL) and washed with water (15 mL). The organic phase was dried over sodium sulfate, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with ethyl acetate/*n*-heptane to yield the titled compound.

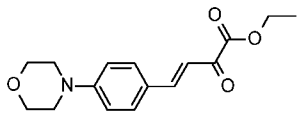
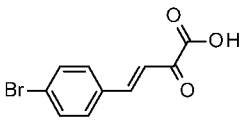
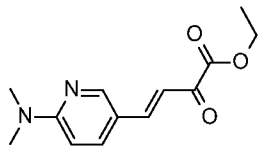
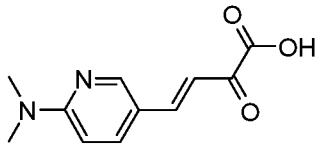
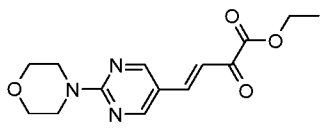
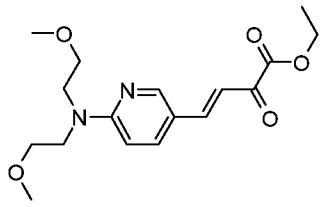
Table VII. List of alkylidene pyruvates

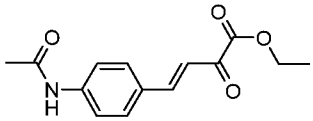
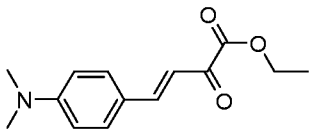
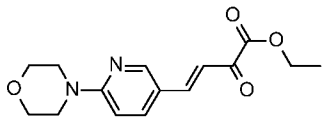
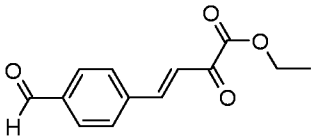
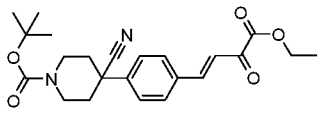
Int.	Structure	Name	SM	method	MW	Mes
ALP01		(*E*)-4-(4-morpholinophenyl)-2-oxo-but-3-enoic acid	1204-86-0	G1	261	262

Int.	Structure	Name	SM	method	MW	Mes
ALP02		(*E*)-4-[4-(dimethylamino) phenyl]-2-oxo-but-3-enoic acid	100-10-7	G1	219	220
ALP03		(*E*)-4-[2-(dimethylamino) pyrimidin-5-yl]-2-oxo-but-3-enoic acid	55551-49-0	G1	221	222
ALP04		(*E*)-4-(2-morpholinopyrimidin-5-yl)-2-oxo-but-3-enoic acid	842974-69-0	G1	263	264
ALP05		(*E*)-4-(6-morpholino-3-pyridyl)-2-oxo-but-3-enoic acid	173282-60-5	G1	262	263
ALP06		(*E*)-4-(4-methoxyphenyl) -2-oxo-but-3-enoic acid	123-11-5	G1	206	207
ALP07		(*E*)-4-(6-Chloro-pyridin-3-yl)-2-oxo-but-3-enoic acid	23100-12-1	G1	211-213	212-214

Int.	Structure	Name	SM	method	MW	Mes
ALP08		ethyl (*E*)-4-[6-[2-methoxyethyl(methyl)amino]-3-pyridyl]-2-oxo-but-3-enoate	ALD01	G2	291	292
ALP09		ethyl (*E*)-4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-2-oxo-but-3-enoate	ALD02	G2, Specific example	313	314
ALP10		ethyl (*E*)-4-[6-[methyl(tetrahydropyran-4-yl)amino]-3-pyridyl]-2-oxo-but-3-enoate	ALD03	G2	318	319
ALP11		ethyl (*E*)-4-[4-[2-methoxyethyl(methyl)amino]phenyl]-2-oxo-but-3-enoate	ALD04	G2	291	292
ALP12		ethyl (*E*)-4-[4-(4-cyano-1-piperidyl)phenyl]-2-oxo-but-3-enoate	ALD 05	G2	312	313

Int.	Structure	Name	SM	method	MW	Mes
ALP13		ethyl (*E*)-4-[2-[methyl(tetrahydropyran-4-yl)amino]pyrimidin-5-yl]-2-oxo-but-3-enoate	ALD06	G2	319	320
ALP14		ethyl (*E*)-4-[2-(4-cyano-1-piperidyl)pyrimidin-5-yl]-2-oxo-but-3-enoate	ALD07	G2	314	315
ALP15		ethyl (*E*)-4-[4-[methyl(tetrahydropyran-4-yl)amino]phenyl]-2-oxo-but-3-enoate	ALD08	G2	317	318
ALP16		ethyl (*E*)-4-[2-[2-methoxyethyl(methyl)amino]pyrimidin-5-yl]-2-oxo-but-3-enoate	ALD09	G2	293	294
ALP17		ethyl (*E*)-4-(2,6-difluoro-4-methoxy-phenyl)-2-oxo-but-3-enoate	256417-10-4	G2	270	271

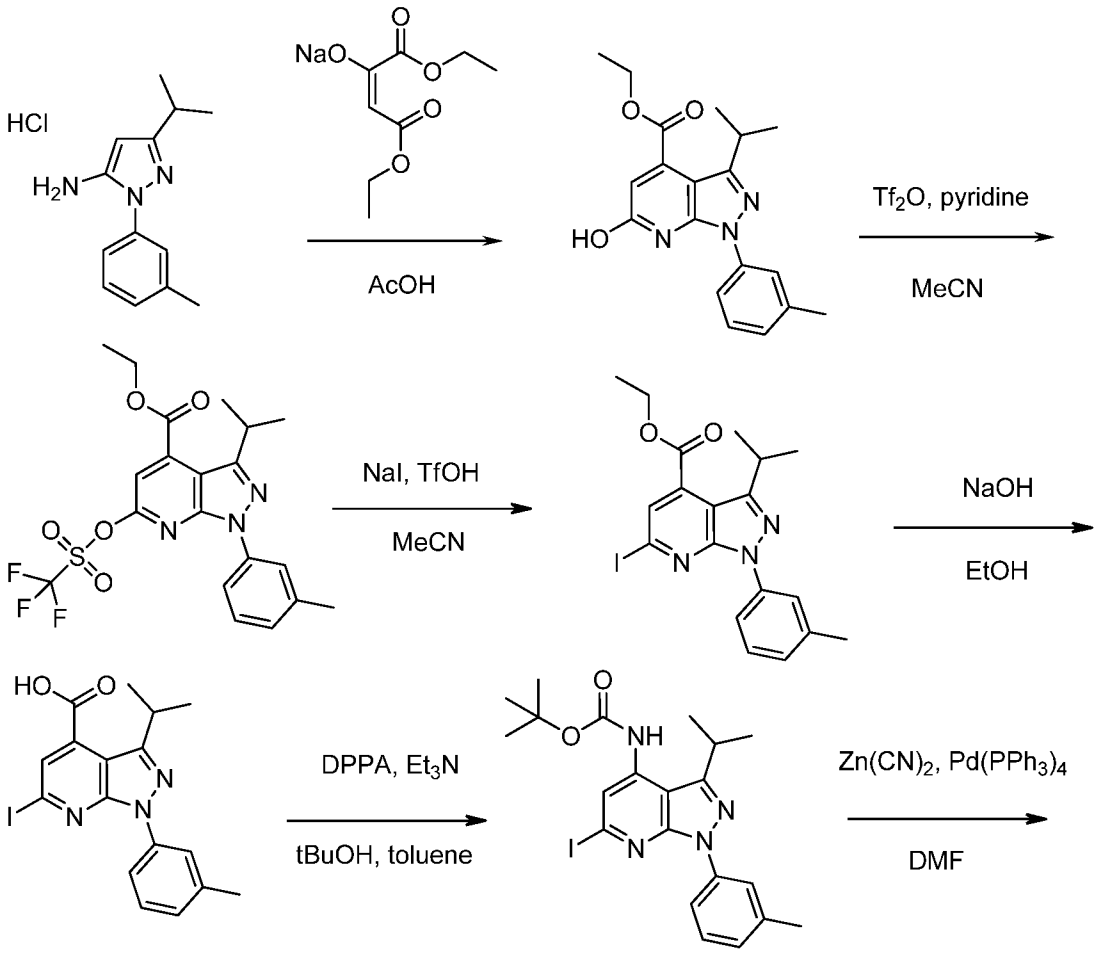
Int.	Structure	Name	SM	method	MW	Mes
ALP18		(*E*)-4-(4-Morpholin-4-yl-phenyl)-2-oxo-but-3-enoic acid ethyl ester	ALD11, 1204-86-0	G2	289	290
ALP19		(*E*)-4-(4-Bromo-phenyl)-2-oxo-but-3-enoic acid	1122-91-4	G1, Specific example	254-256	255-257
ALP20		(*E*)-4-(6-Dimethylamino-pyridin-3-yl)-2-oxo-but-3-enoic acid ethyl ester	ALD10	G2	248	249
ALP21		(*E*)-4-(6-Dimethylamino-pyridin-3-yl)-2-oxo-but-3-enoic acid	ALD10	G1	220	221
ALP22		(*E*)-4-(2-Morpholin-4-yl-pyrimidin-5-yl)-2-oxo-but-3-enoic acid ethyl ester	842974-69-0	G2	291	292
ALP23		(*E*)-4-{6-[Bis-(2-methoxy-ethyl)-amino]-pyridin-3-yl}-2-oxo-but-3-enoic acid ethyl ester	ALD12	G2	336	337

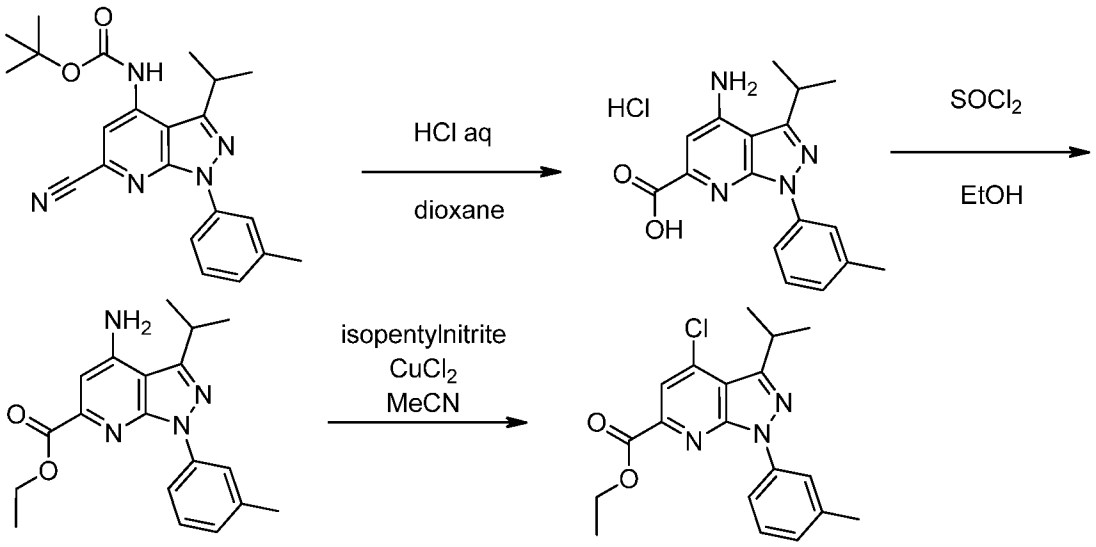
Int.	Structure	Name	SM	method	MW	Mes
ALP24		(*E*)-4-(4-Acetylamino-phenyl)-2-oxo-but-3-enoic acid ethyl ester	122-85-0	G2	261	262
ALP25		(*E*)-4-(4-Dimethylamino-phenyl)-2-oxo-but-3-enoic acid ethyl ester	100-10-7	G2	247	248
ALP26		(*E*)-4-(6-Morpholin-4-yl-pyridin-3-yl)-2-oxo-but-3-enoic acid ethyl ester	173282-60-5	G2	290	291
ALP36		ethyl 4-(4-formylphenyl)-2-oxobut-3-enoate	63697-96-1	G3, Specific example	232	
ALP38		4-Cyano-4-[4-((*E*)-3-ethoxycarbonyl-3-oxo-propenyl)-phenyl]-piperidine-1-carboxylic acid *tert*-butyl ester	847615-14-9	Specific example	412	NA

Methods H1-H3: Synthesis of halogenated pyrazolopyridine

Method H1: Synthesis of halogenated pyrazolopyridine (route 1)

Illustrative synthesis of HP01: ethyl 4-chloro-3-isopropyl-1-(m-tolyl)pyrazolo[3,4-b]pyridine-6-carboxylate





[00380] *Step 1: 6-Hydroxy-3-isopropyl-1-m-tolyl-1H-pyrazolo[3,4-b]pyridine-4-carboxylic acid ethyl ester*

[00381] 5-Isopropyl-2-*m*-tolyl-2*H*-pyrazol-3-ylamine hydrochloride (AMP07, 14.97 g, 59.7 mmol) was dissolved in AcOH (100 mL). Diethyloxalacetate sodium salt (CAS: 40876-98-0, 15 g, 71.6 mmol, 1.2 equiv) was added, and the reaction mixture was refluxed overnight. The reaction mixture was cooled down to RT, poured into water (400 mL) and diluted with ethyl acetate. The two phases were separated, and the aqueous phase was extracted with ethyl acetate. The combined organic layers were concentrated in vacuo, and the resulting residue was taken up twice with cyclohexane (2×200 mL) and concentrated in vacuo again. The residue was suspended in a mixture of ethanol/water (100 mL/20 mL), and the resulting precipitate was collected by filtration and washed with heptane. The solid was dried under vacuum to provide the titled compound.

[00382] *Step 2: 3-Isopropyl-1-m-tolyl-6-trifluoromethanesulfonyloxy-1H-pyrazolo[3,4-b]pyridine-4-carboxylic acid ethyl ester*

[00383] 6-Hydroxy-3-isopropyl-1-*m*-tolyl-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid ethyl ester (14.25 g, 42 mmol) was suspended in acetonitrile under nitrogen atmosphere. Pyridine (3.8 mL, 46.2 mmol, 1.1 equiv) was added. The reaction mixture was cooled to 0 °C, and trifluoromethanesulfonic anhydride (CAS 358-23-6, 7.8 mL, 46.2 mmol, 1.1 equiv) was added dropwise over 20 min. The reaction mixture was then warmed up to RT over 20 min. Water was added (200 mL), and the suspension was filtered. The solid was washed successively with water and ethanol (40 mL) and then dried in vacuo to afford the titled compound.

[00384] *Step 3*: *6-Iodo-3-isopropyl-1-m-tolyl-1H-pyrazolo[3,4-b]pyridine-4-carboxylic acid ethyl ester*

[00385] 3-Isopropyl-1-*m*-tolyl-6-trifluoromethanesulfonyloxy-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid ethyl ester (13.0 g, 27.6mmol) was suspended in acetonitrile. Sodium iodide (20.7 g, 138 mmol, 5 equiv) was added. The reaction mixture was cooled to 0 °C, trifluoromethanesulfonic acid (5.4 mL, 60.7 mmol, 2.2 equiv) was added dropwise. The reaction mixture was stirred at RT overnight. At this point, the reaction was not complete and additional trifluoromethanesulfonic acid (2 mL, 22.6 mmol,0.8 equiv) was added and stirring was continued for 1 hour. Water was added to the reaction mixture, and the suspension was filtered. The solid was washed with ethanol (10 mL) and dried in vacuo to afford the titled compound.

[00386] *Step 4*: *6-Iodo-3-isopropyl-1-m-tolyl-1H-pyrazolo[3,4-b]pyridine-4-carboxylic acid*

[00387] 6-Iodo-3-isopropyl-1-*m*-tolyl-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid ethyl ester (8.73 g, 4.63 mmol) was suspended in ethanol (10 mL). An aqueous solution of 2 M sodium hydroxide (10 mL, 20 mmol, 4.3 equiv) was added, and the reaction mixture was stirred at 70 °C until complete conversion. Then the reaction mixture was cooled down to 0 °C, and an aqueous solution of 2 M HCl was added until pH < 2 was reached. The resulting suspension was filtered, and the solid was dried in vacuo to afford the titled compound.

[00388] *Step 5*: *(6-Iodo-3-isopropyl-1-m-tolyl-1H-pyrazolo[3,4-b]pyridin-4-yl)-carbamicacid tert-butyl ester*

[00389] 6-Iodo-3-isopropyl-1-*m*-tolyl-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (8.12 g, 19.3 mmol) was suspended in toluene (43 mL). *tert*-Butanol (3.1 mL, 32.6 mmol, 2.0 equiv), triethylamine (4.54 mL, 32.6 mmol, 2.0 equiv) and diphenylphosphoryl azide (CAS 26386-88-9, 5 mL, 23.1 mmol, 1.2 equiv) were successively added. The reaction mixture was refluxed for 30 minutes. The reaction mixture was cooled down to RT and partitioned between ethyl acetate and water. The aqueous phase was further extracted with ethyl acetate. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated in vacuo. The residue was suspended in ethanol. The resulting precipitate was collected by filtration, washed with ethanol and dried under vacuum to provide the titled compound.

[00390] *Step 6*: *(6-Cyano-3-isopropyl-1-m-tolyl-1H-pyrazolo[3,4-b]pyridin-4-yl)-carbamic acid tert-butyl ester*

[00391] (6-Iodo-3-isopropyl-1-*m*-tolyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl)-carbamicacid *tert*-butyl ester (7.56 g, 15.4 mmol) was solubilized in dry dimethylformamide (20 mL) in a sealed vial. Zinc cyanide (CAS 557-21-1, 1.1 g, 9.2 mmol, 0.6 equiv) was added, and the reaction mixture was degassed with argon (bubbling) for 5 minutes. Tetrakis(triphenylphosphine)palladium(0) (CAS 14221-01-3, 0.9 g, 0.77 mmol, 0.05 equiv) was added, and the reaction mixture was degassed again with argon (bubbling) for 5 minutes. The vial was sealed, and the reaction mixture was stirred at 110 °C for 2 hour. The reaction mixture was cooled down to room temperature and diluted with water and ethyl acetate. The aqueous phase was further extracted with ethyl acetate. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated to a volume of 10 mL. Ethanol (10 mL) was added, and the suspension was stirred at 0 °C for 10 min. The resulting precipitate was collected by filtration, washed with ethanol and dried under vacuum to provide the titled compound.

[00392] *Step 7*: *4-Amino-3-isopropyl-1-m-tolyl-1H-pyrazolo[3,4-b]pyridine-6-carboxylic acid hydrochloride salt*

[00393] (6-Cyano-3-isopropyl-1-*m*-tolyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl)-carbamic acid *tert*-butyl ester (4.8 g, 12.26 mmol) was suspended in 6 M HCl (50 mL). The reaction mixture was refluxed for 24 h. The reaction mixture was cooled to 0 °C, and the obtained suspension was filtered. The solid was washed with diisopropyl ether and dried in vacuo to yield the titled compound.

[00394] *Step 8*: *4-Amino-3-isopropyl-1-m-tolyl-1H-pyrazolo[3,4-b]pyridine-6-carboxylic acid ethyl ester*

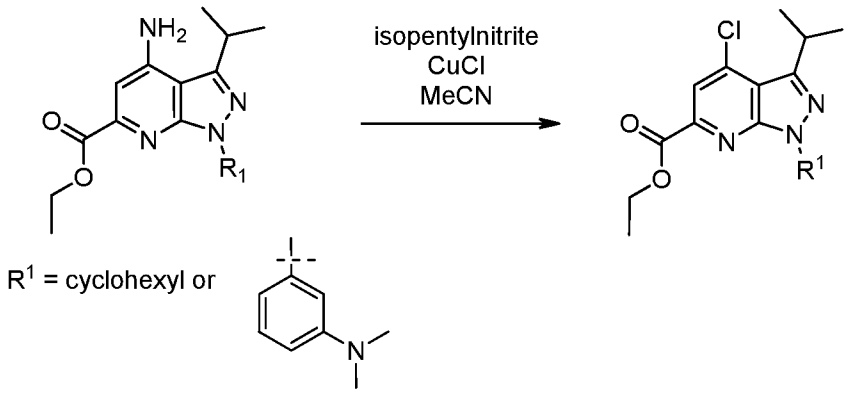
[00395] 4-Amino-3-isopropyl-1-*m*-tolyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid hydrochloride salt (4.23 g, 12.26 mmol) was solubilized in ethanol (150 mL). Thionyl chloride (CAS 7719-09-7, 1.34 mL, 18.39 mmol, 1.5 equiv) was carefully added. The reaction mixture was refluxed for 24 hours. The reaction mixture was cooled down to RT and concentrated in vacuo. The residue was taken up in ethanol (85 mL) and thionyl chloride (CAS 7719-09-7, 2.32 mL, 31.86 mmol, 2.6 equiv) was carefully added at RT. The mixture was refluxed for 6 hours. The reaction mixture was cooled down to RT and concentrated in vacuo. The crude mixture was diluted with ethyl acetate, basified with a saturated solution of sodium hydrogencarbonate. This mixture was filtered through a pad of Celpure® P65. Solids were washed with ethyl acetate. The two phases of the filtrate were separated, and the aqueous fraction was further extracted with

ethyl acetate. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (eluent system : heptane / ethyl acetate gradient from 95/5 to 80/20) to afford the titled compound.

[00396] *Step 9*: *4-Chloro-3-isopropyl-1-m-tolyl-1H-pyrazolo[3,4-b]pyridine-6-carboxylic acid ethyl ester*

[00397] Copper (II) chloride (CAS 7447-39-4, 1.045 g, 7.77 mmol, 1.0 equiv) was suspended in acetonitrile (33 mL). Isopentylnitrite (CAS 110-46-3, 1.57 mL, 11.65 mmol, 1.5 equiv) was added, and the reaction mixture was stirred at RT for 30 minutes. 4-Amino-3-isopropyl-1-*m*-tolyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid ethyl ester (2.63 g, 7.77 mmol, 1.0 equiv) was added. The reaction mixture was stirred at 75 °C for 2.5 h. The reaction mixture was cooled down to 0 °C, and the resulting suspension was filtered. The solid was washed with cold acetonitrile and dried in vacuo to afford the titled compound. The filtrate was concentrated in vacuo and purified by flash chromatography on silica gel (eluent system: heptane /ethyl acetate gradient from 100/0 to 98/2) to provide additional titled compound.

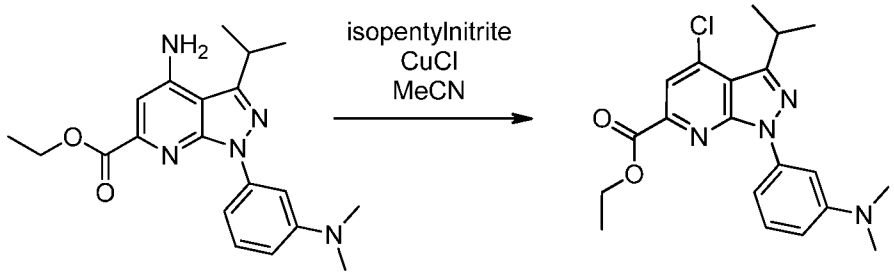
Method H1': Alternative conditions for chlorination route 1 step 9



[00398] To the 4-amino intermediate (1 equiv) in acetonitrile at RT is added isopentylnitrite (CAS 110-46-3, from 3 to 6 eq) followed by copper(I) chloride (CAS 7758-89-6, from 3 to 6 equiv), and the reaction mixture is stirred at RT for 1 h to 24 h. The reaction mixture is diluted with dichloromethane and with a saturated solution of sodium hydrogencarbonate. The two phases are separated, and the aqueous phase is extracted with dichloromethane. The combined organic phases are washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo.

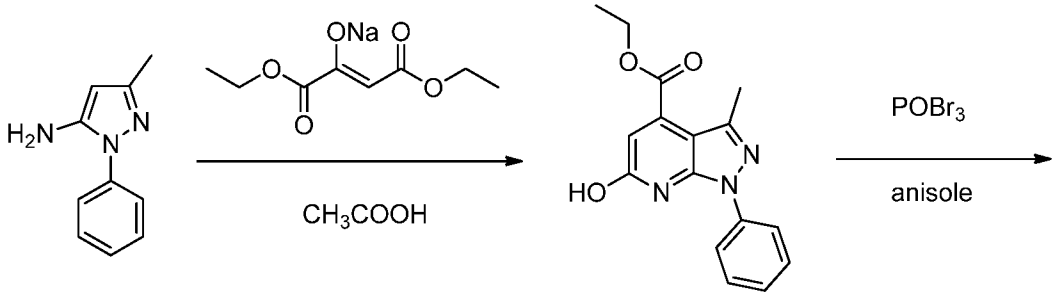
The resulting residue is purified by flash chromatography on silica gel to afford the titled compound.

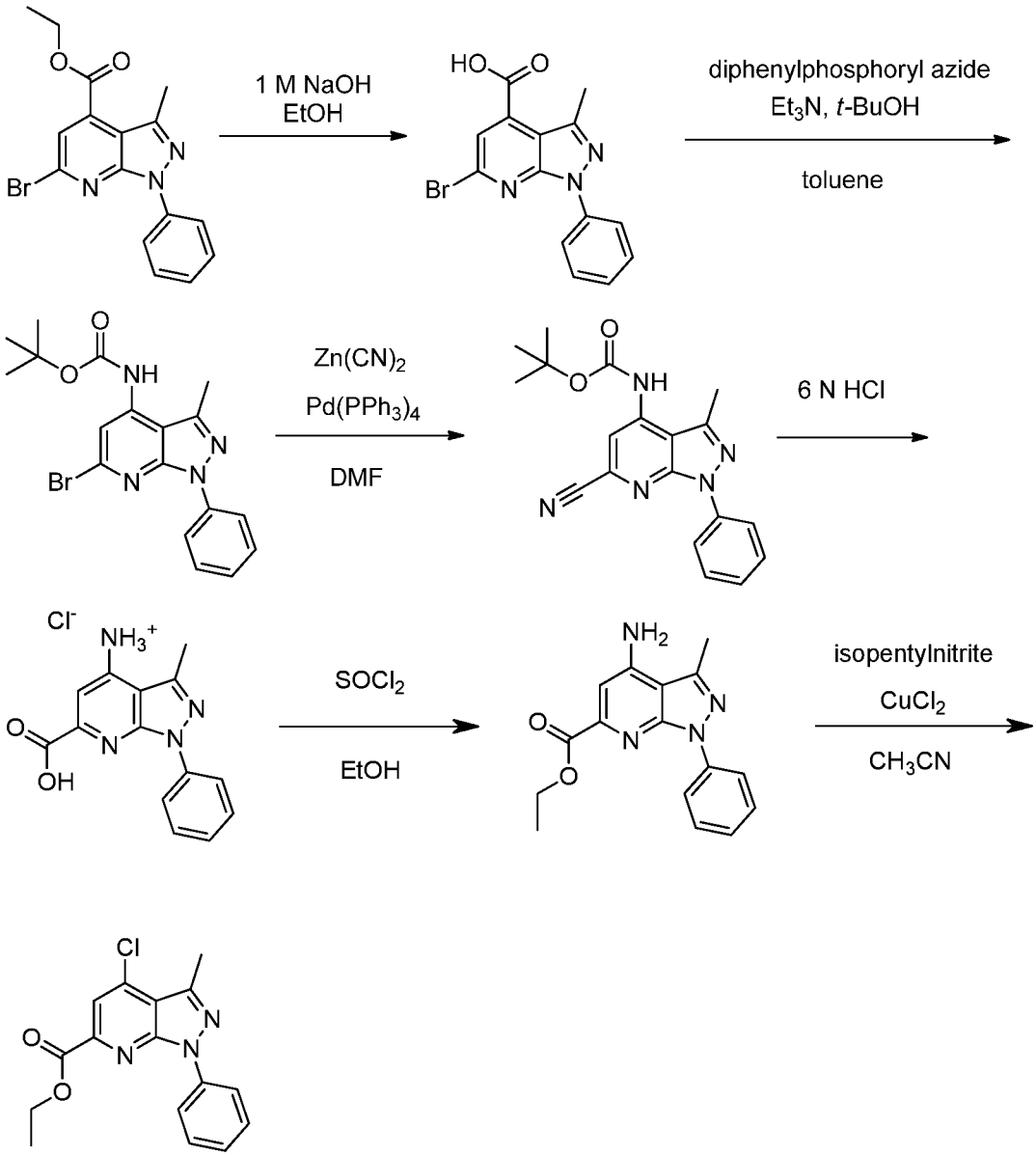
Illustrative synthesis of HP03 : ethyl 4-chloro-1-[3-(dimethylamino)phenyl]-3-isopropyl-pyrazolo[3,4-b]pyridine-6-carboxylate



[00399] To 4-amino-1-(3-dimethylamino-phenyl)-3-isopropyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid ethyl ester (1 g, 2.74 mmol, 1 equiv) in acetonitrile (10 mL) at RT was added isopentylnitrite (CAS 110-46-3, 1.1 mL, 8.21 mmol, 3 equiv) followed by copper(I) chloride (CAS 7758-89-6, 0.82 g, 8.21 mmol, 3 equiv), and the reaction mixture was stirred at RT for 1 h. The reaction mixture was diluted with dichloromethane and with a saturated solution of sodium hydrogencarbonate. The two phases were separated, and the aqueous phase was extracted with dichloromethane. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting residue was purified by flash chromatography on silica gel (eluent system: heptane/ethyl acetate gradient from 100/0 to 90/10) to afford the titled compound.

Synthesis of HP13: ethyl 4-chloro-3-methyl-1-phenyl-pyrazolo[3,4-b]pyridine-6-carboxylate





[00400] *Step 1: 6-Hydroxy-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-4-carboxylic acid ethyl ester*

[00401] 5-Amino-3-methyl-1-phenylpyrazole (CAS: 1131-18-6, 6.83 g, 39.4 mmol) was dissolved in AcOH (70 mL). Diethyloxalacetate sodium salt (CAS: 40876-98-0, 9.12 g, 44.4 mmol, 1.1 equiv) was added, and the reaction mixture was refluxed until complete conversion. The reaction mixture was concentrated in vacuo, and the residue was taken up in cyclohexane (2×100 mL) and concentrated in vacuo again. The residue was suspended in a mixture of MeOH/water (150 mL/100 mL). The resulting precipitate was collected by filtration and washed with heptane. The solid was dried under vacuum to provide the titled compound.

[00402] *Step 2: 6-Bromo-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-4-carboxylic acid ethyl ester*

[00403] 6-Hydroxy-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid ethyl ester (7.27 g, 24.5 mmol) was solubilized in anisole (30 mL). Phosphorous(V) oxybromide (CAS 7789-59-5, 8.23 g, 29.3 mmol, 1.2 equiv) was added, and the reaction mixture was refluxed at 140 °C for 1 h. The reaction mixture was cooled down to room temperature and basified with a saturated solution of sodium hydrogencarbonate. The reaction mixture was extracted twice with ethyl acetate, and the combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by filtration on a pad of silica gel (200 g), heptane/EtOAc 100/0 to 90/10) to give the titled compound.

[00404] *Step 3: 6-Bromo-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-4-carboxylic acid*

[00405] 6-Bromo-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid ethyl ester (3.90 g, 10.8 mmol) was suspended in ethanol (20 mL). An aqueous solution of 1 M sodium hydroxide (20 mL, 20 mmol, 1.9 equiv) was added, and the reaction mixture was stirred at 70 °C for 30 min. The reaction mixture was then concentrated in vacuo. The residue was acidified with an aqueous solution of 2 M HCl and extracted with ethyl acetate. The organic phase was dried over Na_2SO_4, filtered and concentrated in vacuo to yield the titled compound.

[00406] *Step 4: (6-Bromo-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridin-4-yl)-carbamic acid tert-butyl ester*

[00407] 6-Bromo-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-4-carboxylic acid (3.50 g, 10.4 mmol) was suspended in toluene (35 mL). *tert*-Butanol (2 mL, 21.6 mmol, 2.1 equiv), triethylamine (4.4 mL, 31.2 mmol, 3.0 equiv) and diphenylphosphoryl azide (CAS 26386-88-9, 3.2 mL, 14.8 mmol, 1.4 equiv) were successively added. The reaction mixture was refluxed for 1.5 h. The reaction mixture was cooled down to RT and concentrated in vacuo, then partitioned between ethyl acetate and water. The aqueous phase was further extracted with ethyl acetate. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by filtration on a pad of silica gel (200 g, heptane/EtOAc 100/0 to 90/10) to give the titled compound.

[00408] *Step 5: (6-Cyano-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridin-4-yl)-carbamic acid tert-butyl ester*

[00409] (6-Bromo-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl)-carbamic acid *tert*-butyl ester (4.16 g, 10.3 mmol) was solubilized in dry dimethylformamide (20 mL) in a sealed vial. Zinc cyanide (CAS 557-21-1, 0.727 g, 6.2 mmol, 0.6 equiv) was added, and the reaction mixture was degassed with argon for 5 minutes. Tetrakis(triphenylphosphine) palladium(0) (CAS 14221-01-3, 0.595 g, 0.5 mmol, 0.05 equiv) was added, and the vial was sealed. The reaction mixture was stirred at 100 °C for 1 hour. The reaction was not complete. Additional tetrakis(triphenylphosphine)palladium(0) (CAS 14221-01-3, 0.595 g, 0.5 mmol, 0.05 equiv) and zinc cyanide (CAS 14221-01-3, 0.485 g, 4.1 mmol, 0.4 equiv) were added at RT, and the vial was sealed again. The reaction mixture was stirred at 100 °C for one hour and cooled down to room temperature. Water was added to the reaction mixture and precipitation occurred. The suspension was filtered, and the cake was washed with water. The solid residue was taken up with dichloromethane and with an aqueous solution of 0.5 M NaOH. The organic phase was separated, dried over Na_2SO_4, filtered and concentrated. The residue was purified by filtration on a pad of silica gel (150 g, heptane/EtOAc 100/0 to 60/40) to give the titled compound mixed with (6-cyano-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl)-carbonitrile. The mixture was engaged in the next step without further purification.

[00410] *Step 6: 4-Amino-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxylic acid hydrochloride salt*

[00411] A mixture of (6-cyano-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl)-carbamic acid *tert*-butyl ester and (6-cyano-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl)-carbonitrile (3.5 g) was suspended in 6 M HCl (50 mL). The reaction mixture was refluxed for 18 h. The reaction mixture was cooled to 0 °C and the obtained suspension was filtered. The solid was washed with an aqueous solution of 0.1 M HCl. The filtrate was concentrated in vacuo and precipitation occurred. The solid was also collected by filtration. The combined solids were dried in vacuo to yield the titled compound.

[00412] *Step 7: 4-Amino-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxylic acid ethyl ester*

[00413] 4-Amino-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid hydrochloride salt (2.03 g, 7.6 mmol) was solubilized in ethanol (40 mL). Thionyl chloride (CAS 7719-09-7, 1.16 mL, 15.9 mmol, 2.1 equiv) was carefully added. The reaction mixture was refluxed for 24 hours. The reaction mixture was concentrated in vacuo and partitioned

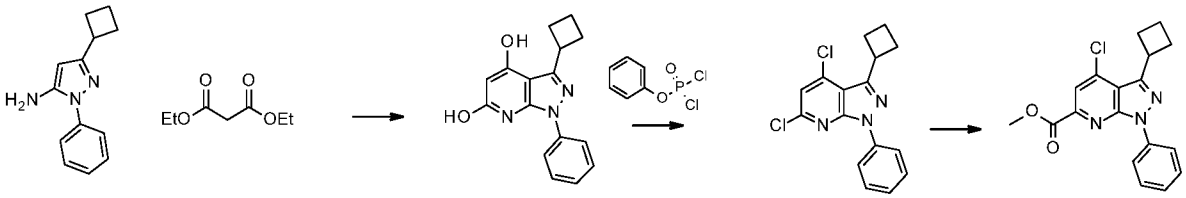
between ethyl acetate and aqueous saturated $NaHCO_3$. The aqueous phase was further extracted with ethyl acetate. The combined organic phases were dried over Na_2SO_4, filtered and concentrated in vacuo to give the titled compound.

[00414] *Step 8: 4-Chloro-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxylic acid ethyl ester*

[00415] Copper (II) chloride (CAS 7447-39-4, 0.908 g, 6.75 mmol, 1.0 equiv) was added to acetonitrile (50 mL). Isopentylnitrite (CAS 110-46-3, 1.4 mL, 10.1 mmol, 1.5 equiv) was added, and the reaction mixture was stirred at 75 °C for 5 minutes. 4-Amino-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid ethyl ester (2.0 g, 6.75 mmol, 1.0 equiv) dissolved in acetonitrile (50 mL) was added. The reaction mixture was stirred at 75 °C for 2.5 h. The reaction mixture was cooled down and concentrated in vacuo. Water was added to the residue, and the mixture was extracted with ethyl acetate. Copper salts prevented clean extraction. The suspension was filtered through diatomaceous earth. The organic phase was dried over Na_2SO_4, filtered and concentrated. The residue was suspended in ethanol (10 mL) and filtered. The solid was dried in vacuo to give the titled compound. The copper salts on the diatomaceous earth were washed with dichloromethane. The filtrate was concentrated to provide additional titled compound.

Method H2: Synthesis of halogenated pyrazolopyridine (route 2)

Illustrative synthesis of HP02: methyl 4-chloro-3-cyclobutyl-1-phenyl-pyrazolo[3,4-b]pyridine-6-carboxylate



[00416] *Step 1: 3-cyclobutyl-1-phenyl-pyrazolo[3,4-b]pyridine-4,6-diol*

[00417] To a mixture of 3-cyclobutyl-1-phenyl-1*H*-pyrazol-5-amine (AMP29, 74.0 g, 347 mmol) in oxydibenzene (450.0 g, 2.64 mol) was added diethyl malonate (CAS 105-53-3, 139.0 g, 867 mmol). The system was heated at 130-150 °C for 40 h. By this time solid had precipitated and heating was stopped. Two more reactions were set up as described above. All three reaction mixtures were combined. The combined mixture was cooled to below 40 °C and

diluted with about 1.8 L of diethyl ether, and the resulting suspension was stirred for 2 h and then filtered. The collected solids were rinsed with diethyl ether (1 L). The solids were dried on the filter to give the titled compound. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 11.28 (s, 1H), 8.18 (d, J=7.9 Hz, 2H), 7.58 - 7.39 (m, 2H), 7.21 (t, J=7.1 Hz, 1H), 5.85 (s, 1H), 3.88 (quin, J=8.4 Hz, 1H), 2.44 - 2.22 (m, 4H), 2.07 - 1.78 (m, 2H).

[00418] *Step 2: 4,6-dichloro-3-cyclobutyl-1-phenyl-pyrazolo[3,4-b]pyridine*

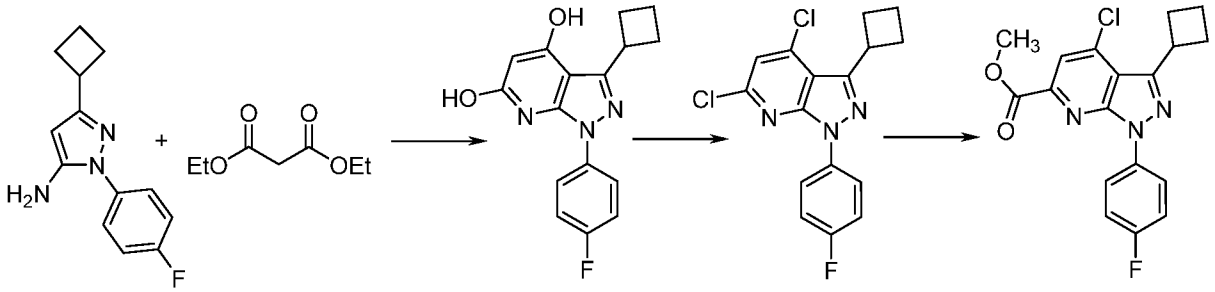
[00419] A mixture of 3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-4,6-diol (60.0 g, 213 mmol) in phenyl dichlorophosphate (CAS 770-12-7,135 g, 640 mmol) was stirred at 170 °C for 15 h. Two more reactions were set up as described above. All three reaction mixtures were combined and poured into ice water (5 L) keeping the internal temperature <10 °C. The mixture was neutralized with concentrated NH_4OH (500 mL) to pH 6~7, then the suspension was stirred for 2 h. As the pH increased and with continued stirring, the semi-solid suspension becomes a flowing solid. The solid was collected by filtration. The wet solid was dissolved in dichloromethane (3 L) and filtered through a short path of silica gel (2 kg), eluting with dichloromethane (15 L). The filtrate was concentrated to a solid which was triturated with acetonitrile (1.5 L) and and collected by filtration to give the titled compound. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.20 (d, J=7.9 Hz, 2H), 7.51 (t, J=7.5 Hz, 2H), 7.35 - 7.27 (m, 1H), 7.16 (s, 1H), 4.15 (quin, J=8.4 Hz, 1H), 2.63 - 2.41 (m, 4H), 2.20 - 2.07 (m, 1H), 2.00 (s, 1H).

[00420] *Step 3: methyl 4-chloro-3-cyclobutyl-1-phenyl-pyrazolo[3,4-b]pyridine-6-carboxylate*

[00421] To a mixture of 4,6-dichloro-3-cyclobutyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine (50.0 g, 157 mmol) in methanol (700 mL) was added triethylamine (31.8 g, 314 mmol) and Pd(dppf)Cl_2•DCM (CAS 95464-05-4, 6.4 g, 7.86 mmol). The system was heated at 60 °C under CO (30 psi) for 40 h. Two more reactions were set up as described above. All three reaction mixtures were combined and concentrated to give a semisolid which was dissolved in dichloromethane (3 L) and filtered through a 2 kg plug of silica gel. After concentration, about 130 g of solid was obtained. This solid was taken up in 1.3 L of ethyl acetate with heating. This solution was stirred at room temperature. Solids came out over a couple of minutes, and then 1.3 L of hexane was added in a thin stream via addition funnel with stirring for 2 hours. The solids were collected by filtration to give the titled compound. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm

8.38 - 8.27 (m, 2H), 7.95 (s, 1H), 7.53 (t, J=7.9 Hz, 2H), 7.35 - 7.27 (m, 1H), 4.21 (q, J=8.6 Hz, 1H), 4.08 - 4.03 (m, 1H), 2.66 - 2.40 (m, 4H), 2.22 - 1.93 (m, 2H).

Illustrative synthesis of HP19: Methyl 4-chloro-3-cyclobutyl-1-(4-fluorophenyl)-1H-pyrazolo[3,4-b]pyridine-6-carboxylate



[00422] *Step 1: 3-Cyclobutyl-1-(4-fluorophenyl)-1H-pyrazolo[3,4-b]pyridine-4,6-diol*

[00423] A mixture of 3-cyclobutyl-1-(4-fluorophenyl)-1*H*-pyrazol-5-amine (AMP93, 5 g, 18.6 mmol) and diethyl malonate ([105-53-3], 8.5 mL, 55.8 mmol) was heated at 100 °C for 30 minutes and then at 170 °C for 3 hours. The reaction mixture was cooled down to RT and dissolved in dichloromethane (60 mL). The resultant solution was poured into a stirred solution of *n*-heptane (700 mL). The precipitate was collected by filtration, washed with *n*-heptane and dried at 40 °C under reduced pressure to give the titled compound.

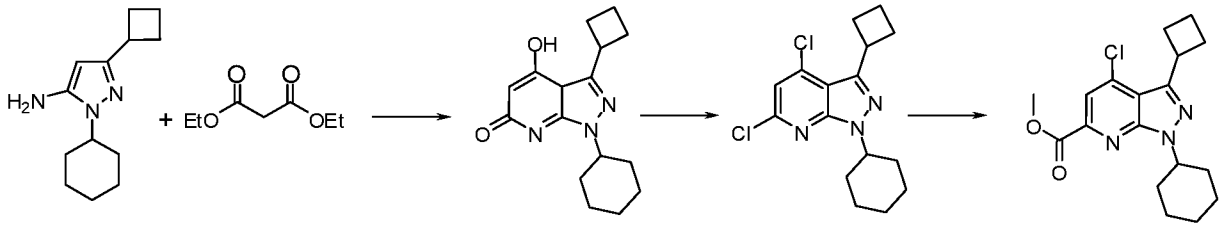
[00424] *Step 2: 4,6-Dichloro-3-cyclobutyl-1-(4-fluorophenyl)-1H-pyrazolo[3,4-b]pyridine*

[00425] A three-neck round-bottom flask equipped with a Dean-Stark apparatus was charged with phenyl dichlorophosphate ([770-12-7], 854 g, 4.05 mol). 3-Cyclobutyl-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-4,6-diol (404 g, 1.35 mol) was added in portions over a period of 5 minutes. The temperature was increased to 170 °C over a period of 1 hour, and the stirring at 170 °C was continued for 21 hours. The reaction mixture was cooled down to 50 °C and added slowly to a stirred aqueous 4 N NaOH (5 L) keeping the temperature below 20 °C. The suspension was stirred for 1 hour at 10-15 °C, and then cold water (3 L) was added. The precipitate was collected by filtration, washed with water and dried at 40 °C under reduced pressure to give the titled compound.

[00426] *Step 3: methyl 4-chloro-3-cyclobutyl-1-(4-fluorophenyl)-1H-pyrazolo[3,4-b]pyridine-6-carboxylate*

[00427] A pressured vessel was charged with 4,6-dichloro-3-cyclobutyl-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine (5 g, 14.9 mmol), Pd(dppf)Cl_2•DCM (CAS 95464-05-4, 218 mg, 0.3 mmol), and sodium acetate (1.8 g, 22.3 mmol) in dioxane/methanol (1:1, 25 mL). The system was loaded with CO (4 bars) and heated at 40 °C for 2 hours. The vessel was cooled to RT, and the conversion was monitored by LCMS. The reaction vessel was charged again with CO (4 bars) and heated at 40 °C. The sequence was repeated until full conversion was observed. The crude mixture was concentrated under reduced pressure and purified by flash column chromatography eluting with a mixture of *n*-heptane/dichloromethane (90/10 to 30/70) to give the titled compound.

*Illustrative synthesis of HP25: methyl 4-chloro-3-cyclobutyl-1-cyclohexyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate*



[00428] *Step 1: 3-cyclobutyl-1-cyclohexyl-4-hydroxy-3aH-pyrazolo[3,4-*b*]pyridin-6-one*

[00429] A mixture of 5-cyclobutyl-2-cyclohexyl-2*H*-pyrazol-3-ylamine (AMP35, 10 g, 45.7 mmol) and diethyl malonate ([105-53-3], 27.7 mL, 183 mmol) in diphenylether (50 mL) was heated at 130 °C over approximately 60 hours. The reaction mixture was cooled down to RT and quenched with 0.5 M NaOH solution (100 mL, 50 mmol). Extraction with EtOAc gave an aqueous phase that was acidified with a 12 M HCl solution (4.3 mL, 51.6 mmol) giving rise to a suspension. This suspension was extracted with EtOAc. The obtained organic layer was dried and concentrated to give the titled compound that was used as such.

[00430] *Step 2: 4,6-dichloro-3-cyclobutyl-1-cyclohexyl-pyrazolo[3,4-b]pyridine*

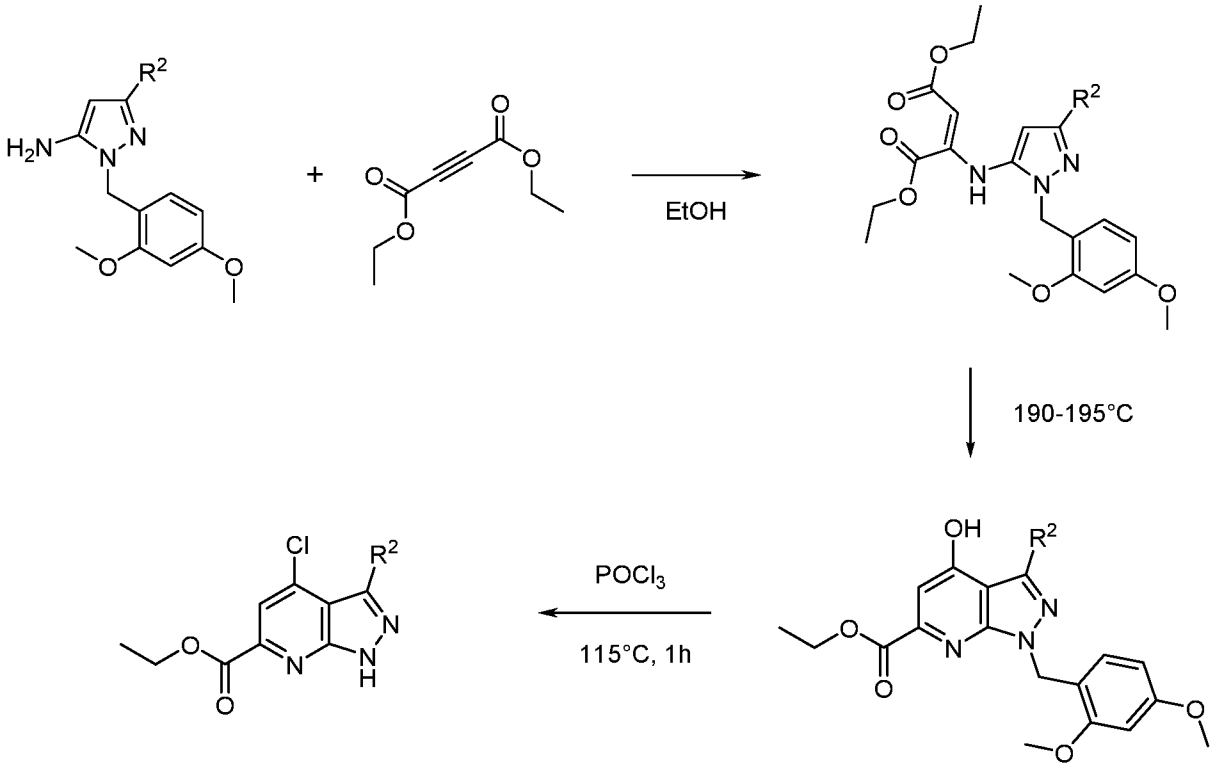
[00431] The 3-cyclobutyl-1-cyclohexyl-4-hydroxy-3aH-pyrazolo[3,4-*b*]pyridin-6-one (5.15 g, 17.9 mmol) was suspended in phenyl dichlorophosphate ([770-12-7], 8.01 mL, 53.8 mmol). The mixture was heated at 130 °C overnight. Next, the mixture was diluted in DCM and poured into ice water. After increasing the pH till 7-8 with a 20% NH_4OH solution, the biphasic mixture was stirred for 30 minutes. Subsequently, the organic phase was separated, dried and concentrated to

give a residue. This residue was purified by chromatography using a petroleum ether/EtOAc gradient (100/0 to 90/10). This resulted in the titled compound that was used as such.

[00432] *Step 3: methyl 4-chloro-3-cyclobutyl-1-cyclohexyl-1H-pyrazolo[3,4-b]pyridine-6-carboxylate*

[00433] In a Parr apparatus, 4,6-dichloro-3-cyclobutyl-1-cyclohexyl-pyrazolo[3,4-*b*]pyridine (2.17 g, 6.72 mmol) was dissolved in MeOH (50 mL) together with $Pd(dppf)Cl_2$•DCM (CAS 95464-05-4, 275 mg, 0.33 mmol) and triethylamine (1.87 mL, 13.4 mmol). The system was loaded with CO (5 bar) and heated at 45 °C for 18 hours. After cooling down the mixture till RT, the mixture was concentrated, and the obtained residue was purified by chromatography using a petroleum ether/EtOAc gradient (100/0 till 95/5). This yielded the titled compound.

Method H3: Synthesis of halogenated or sulfonylated pyrazolopyridine (route 3)



[00434] *Step 1: Diethyl but-2-enedioate*

[00435] To a suspension of aminopyrazole (1 equiv) in ethanol (150 mL) is added diethyl acetylenedicarboxylate (1.1 equiv). The reaction mixture is stirred at room temperature for 4 hours. The reaction mixture is concentrated. The crude residue is purified by silica gel column chromatography (heptane/EtOAc 100/0 to 70/30) to give the titled compound.

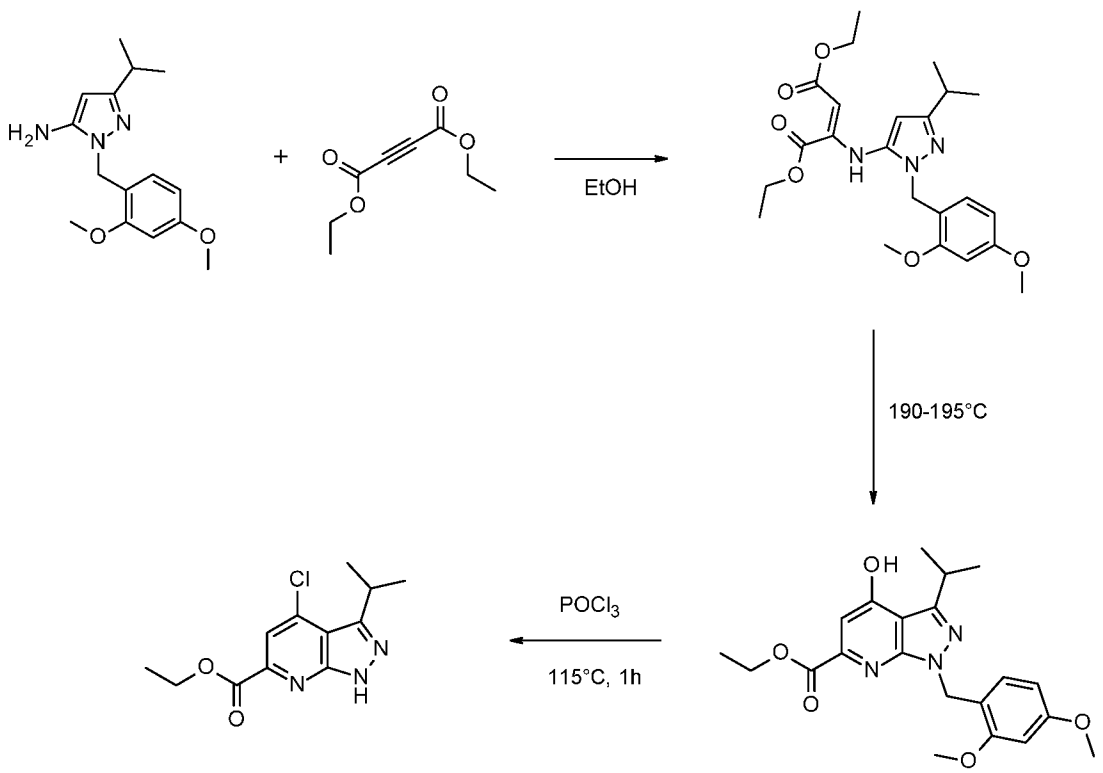
[00436] *Step 2: Pyrazolopyridine formation*

[00437] The diethyl but-2-enedioate is heated under air atmosphere at 190-195 °C for one hour. The reaction mixture is cooled to room temperature and is partitioned between dichloromethane and water. The aqueous phase is separated and extracted two times with dichloromethane. The combined organic phases were dried, filtered and concentrated in vacuo. The crude residue can be purified by silica gel column chromatography to provide the pyrazolopyridine.

[00438] *Step 3: Chlorination*

[00439] A solution of the above pyrazolopyridine (1 equiv) in phosphorus(V) oxychloride (32 equiv) was stirred at 115 °C for 1 h. The reaction mixture is then cooled to room temperature and concentrated in vacuo. The residue is dissolved in ethyl acetate, and the reaction mixture is added dropwise to a solution of saturated of sodium hydrogencarbonate till total neutralization of phosphorus(V) oxychloride (pH 8). The aqueous phase is separated and extracted two times with ethyl acetate. The combined organic phases are washed with brine, dried, filtered and concentrated in vacuo. The crude residue can be purified by silica gel column chromatography to provide the chlorinated pyrazolopyridine from which the dimethoxybenzyl group has also been removed.

Illustrative synthesis of HP08: 4-Chloro-3-isopropyl-1H-pyrazolo[3,4-b]pyridine-6-carboxylic acid ethyl ester



[00440] *Step 1: 2-[2-(2,4-Dimethoxy-benzyl)-5-isopropyl-2H-pyrazol-3-ylamino]-but-2-enedioic acid diethyl ester*

[00441] To a suspension of 2-(2,4-dimethoxy-benzyl)-5-isopropyl-2*H*-pyrazol-3-ylamine (AMP28, 18.14 g, 65.88 mmol) in ethanol (150 mL) was added diethyl acetylenedicarboxylate (CAS: 762-21-0, 11.60 mL, 72.47 mmol). The reaction mixture was stirred at room temperature for 4 hours. The reaction mixture was concentrated. The crude residue was purified by silica gel column chromatography (heptane/EtOAc 100/0 to 70/30) to give the titled compound.

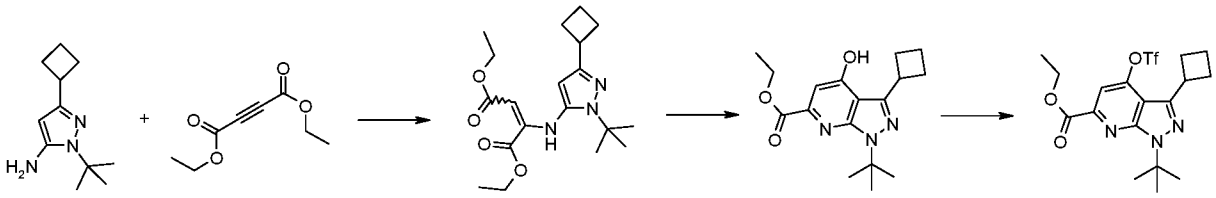
[00442] *Step 2: Compound HP06: 1-(2,4-Dimethoxy-benzyl)-4-hydroxy-3-isopropyl-1H-pyrazolo[3,4-b]pyridine-6-carboxylic acid ethyl ester*

[00443] 2-[2-(2,4-Dimethoxy-benzyl)-5-isopropyl-2*H*-pyrazol-3-ylamino]-but-2-enedioic acid diethyl ester (13.46 g, 30.21 mmol) was heated under air atmosphere at 190-195 °C for one hour. The reaction mixture cooled to room temperature and was partitioned between dichloromethane and water. The aqueous phase was separated and extracted two times with dichloromethane. The combined organic phases were dried over $MgSO_4$, filtered and concentrated in vacuo. The crude residue was purified by silica gel column chromatography (heptane/EtOAc 100/0 to 60/40) to provide the titled compound.

[00444] *Step 3: Compound HP08: 4-Chloro-3-isopropyl-1H-pyrazolo[3,4-b]pyridine-6-carboxylic acid ethyl ester*

[00445] A solution of 1-(2,4-dimethoxy-benzyl)-4-hydroxy-3-isopropyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid ethyl ester (HP06, 4.02 g, 10.06 mmol) in phosphorus(V) oxychloride (CAS 100025-87-3, 30 mL, 322 mmol) was stirred at 115 °C for 1 h. The reaction mixture was then cooled to room temperature and concentrated in vacuo. The residue was dissolved in ethyl acetate, and the reaction mixture was added dropwise to a solution of saturated of sodium hydrogencarbonate till total neutralization of phosphorus(V) oxychloride (pH 8). The aqueous phase was separated and extracted two times with ethyl acetate. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The crude residue was purified by silica gel column chromatography (heptane/EtOAc 100/0 to 75/25) to provide the titled compound.

Illustrative Synthesis of HP20: ethyl 1-tert-butyl-3-cyclobutyl-4-[(trifluoromethanesulfonyl)oxy]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate



[00446] *Step 1: diethyl 2-[(1-tert-butyl-3-cyclobutyl-1H-pyrazol-5-yl)amino]but-2-enedioate*

[00447] In an amber round bottom flask, diethyl acetylenedicarboxylate ([762-21-0], 14.8 mL, 87 mmol) was added to a suspension of AMP94 (15.2 g, 78.8 mmol) in ethanol (200 mL). The reaction mixture was stirred at room temperature for 20 hours, and the mixture was concentrated in vacuo. The crude residue was purified by silica gel column chromatography (heptane/dichloromethane 100/0 to 0/100) to give the titled compound.

[00448] *Step 2: ethyl 1-tert-butyl-3-cyclobutyl-4-hydroxy-1H-pyrazolo[3,4-b]pyridine-6-carboxylate*

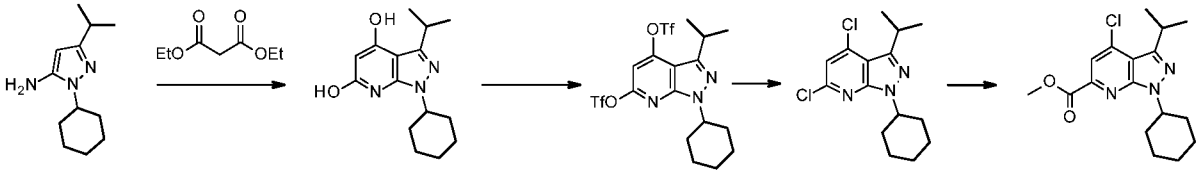
[00449] In a sealed tube, a suspension of diethyl 2-[(1-*tert*-butyl-3-cyclobutyl-1*H*-pyrazol-5-yl)amino]but-2-enedioate (5 g, 13.8 mmol) in Dowtherm® A (5 mL) was heated at 185-190 °C for 24 hours. The reaction mixture was cooled to room temperature and was partitioned between

n-heptane and acetonitrile. The acetonitrile phase was separated and evaporated under reduced pressure. The crude sample was purified by silica gel column chromatography (dichloromethane/n-heptane) to give the titled compound.

[00450] *Step 3: ethyl 1-tert-butyl-3-cyclobutyl-4-[(trifluoromethanesulfonyl)oxy]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate*

[00451] Trifluoromethanesulfonic anhydride ([358-23-6], 1.9 mL, 11.3 mmol) was added dropwise to a solution of ethyl 1-*tert*-butyl-3-cyclobutyl-4-hydroxy-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate (2.5 g, 7.89 mmol) and pyridine (1.9 mL, 23.5 mmol) in acetonitrile (80 mL), maintaining the temperature around 20-25 °C. The reaction mixture was stirred at RT for 20 hours. Then solid sodium hydrogencarbonate and few milliliters of water were added, and the reaction mixture was concentrated in vacuo. The residue was taken up in dichloromethane and water. The two phases were separated, and the aqueous phase was again extracted with dichloromethane. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The resulting residue was purified by silica gel chromatography (n-heptane/ethyl acetate) to yield the titled compound.

Synthesis of HP12: methyl 4-chloro-1-cyclohexyl-3-isopropyl-pyrazolo[3,4-b]pyridine-6-carboxylate



[00452] *Step 1: 1-cyclohexyl-3-isopropyl-pyrazolo[3,4-b]pyridine-4,6-diol*

[00453] A mixture of AMP23 (5.0 g, 24.1 mmol) and diethylmalonate (CAS 105-53, 37.36 mL, 48.2 mmol, 2.0 equiv) was stirred at 190 °C for 2 hours. The reaction mixture was then cooled to RT, and diethyl ether was added. The obtained suspension was filtered; the solid was washed with pentane, and dried in vacuo to give the titled compound.

[00454] *Step 2: [1-cyclohexyl-3-isopropyl-6-(trifluoromethylsulfonyloxy)pyrazolo[3,4-b]pyridin-4-yl] trifluoromethanesulfonate*

[00455] Trifluoromethanesulfonic anhydride (CAS 358-23-6,6.26 mL, 37.2 mmol, 1.75 equiv) was added dropwise at 0 °C to a solution of 1-cyclohexyl-3-isopropyl-pyrazolo[3,4-*b*]pyridine-

4,6-diol (5.85 g, 21.2 mmol) and pyridine (4.3 mL, 53.1 mmol, 2.5 equiv) in acetonitrile (145 mL). The reaction mixture was stirred at RT for 16 hours. Dichloromethane and water were added to the reaction mixture. The two phases were separated, and the organic phase was washed with water and brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was taken up in toluene and concentrated again in vacuo to give the titled compound.

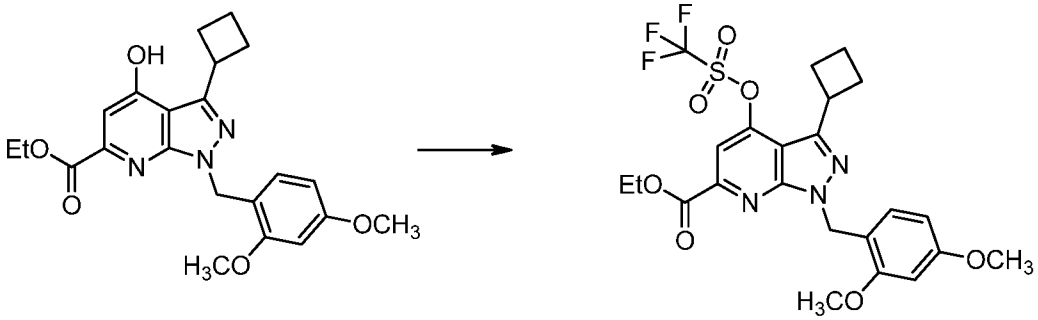
[00456] *Step 3: 4,6-dichloro-1-cyclohexyl-3-isopropyl-pyrazolo[3,4-b]pyridine*

[00457] A mixture of [1-cyclohexyl-3-isopropyl-6-(trifluoromethylsulfonyloxy)pyrazolo[3,4-*b*]pyridin-4-yl] trifluoromethanesulfonate (10.86 g, 20.1 mmol) and 4 N HCl in dioxane (50 mL, 200 mmol, 10 equiv) was stirred at 100 °C for 16 hours in a sealed tube. The reaction mixture was cooled to RT and concentrated in vacuo. The residue was purified by chromatography on silica gel (heptane/dichloromethane 100/0 to 80/20) to yield the titled compound.

[00458] *Step 4: HP12: methyl 4-chloro-1-cyclohexyl-3-isopropyl-pyrazolo[3,4-b]pyridine-6-carboxylate*

[00459] Triethylamine (1.9 mL, 13.6 mmol, 2.0 equiv) and $Pd(dppf)Cl_2$ (CAS : 72287-26-4, 100 mg, 0.14 mmol, 0.02 equiv) were added to a solution of 4,6-dichloro-1-cyclohexyl-3-isopropyl-pyrazolo[3,4-*b*]pyridine (2.13 g, 6.82 mmol) in methanol (55 mL). The system was filled at RT with CO (40 psi) and heated at 100 °C for 1 hour. The reaction mixture was cooled down to RT and concentrated in vacuo. The residue was purified by chromatography on silica gel (heptane/ethyl acetate 100/0 to 90/10) to yield the titled compound.

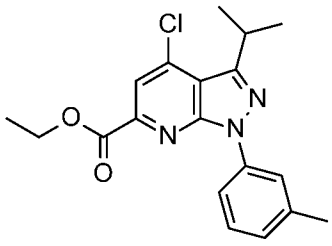
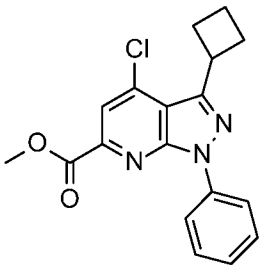
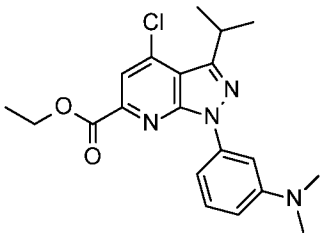
Synthesis of HP14: ethyl 3-cyclobutyl-1-[(2,4-dimethoxyphenyl)methyl]-4-(trifluoromethylsulfonyloxy)pyrazolo[3,4-b]pyridine-6-carboxylate

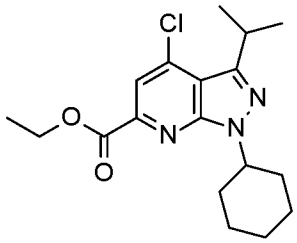
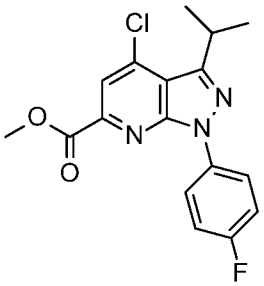
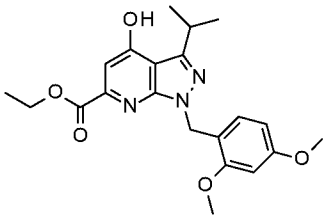
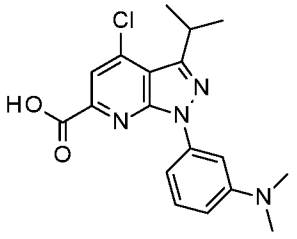


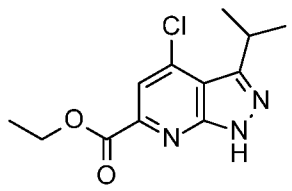
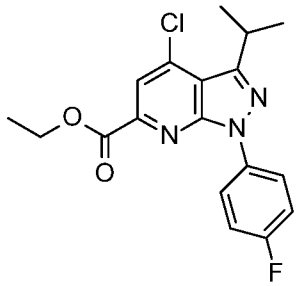
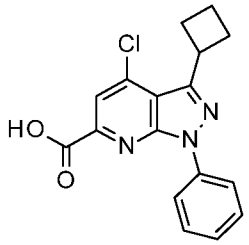
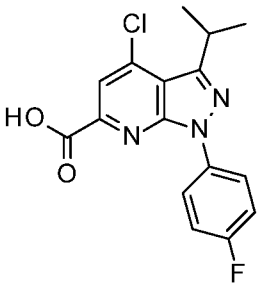
[00460] Trifluoromethanesulfonic anhydride (CAS 358-23-6, 92 µL, 0.56 mmol, 1.45 equiv) was added dropwise at RT to a solution of HP15 (160 mg, 0.39 mmol, 1 equiv) and pyridine (46 µL, 0.58 mmol, 1.5 equiv) in acetonitrile (4 mL). The reaction mixture was stirred at RT for 3 h.

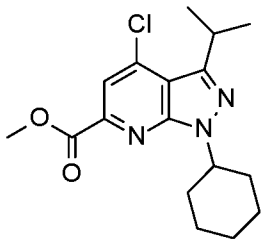
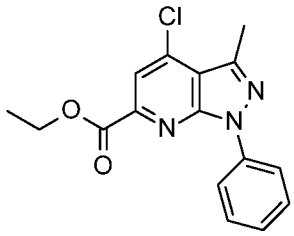
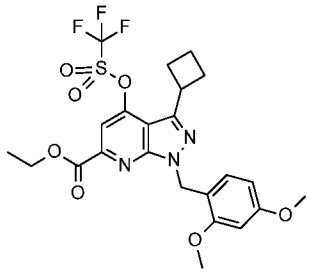
Then solid sodium hydrogencarbonate and few milliliters of water were added, and the reaction mixture was concentrated in vacuo. The residue was taken up in dichloromethane and water. The two phases were separated, and the aqueous phase was extracted with dichloromethane. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting residue was purified by flash chromatography on silica gel (eluent system: heptane/dichloromethane gradient from 100/0 to 0/100) to yield the titled compound.

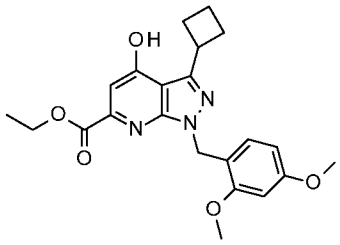
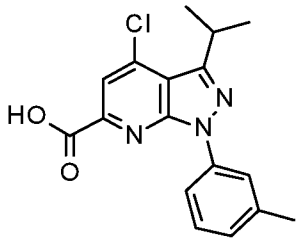
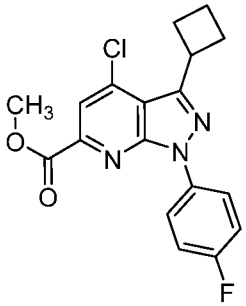
Table VIII. List of halogenated pyrazolopyridine

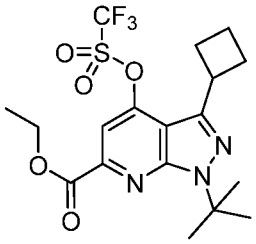
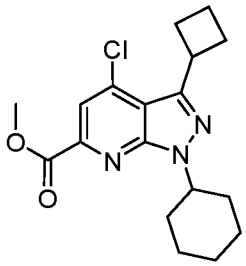
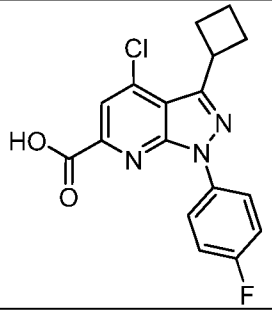
Int.	Structure	Name	SM	method	MW	Mes
HP01		ethyl 4-chloro-3-isopropyl-1-(*m*-tolyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	AMP07	H1 Specific example	357-359	358-360
HP02		methyl 4-chloro-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	AMP29	H2 Specific example	341-343	342-344
HP03		ethyl 4-chloro-1-[3-(dimethylamino)phenyl]-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	AMP06	H1(steps 1 to 8) and H1' (step 9) Specific example	386-388	387-389

Int.	Structure	Name	SM	method	MW	Mes
HP04		ethyl 4-chloro-1-cyclohexyl-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	AMP23	H1(steps 1 to 8) and H1' (step 9)	349-351	350-352
HP05		methyl 4-chloro-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	AMP13	H2	347-349	348-350
HP06		ethyl 1-[(2,4-dimethoxyphenyl)methyl]-4-hydroxy-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	AMP28	H3 (steps 1 & 2 only)	399	400
HP07		4-chloro-1-[3-(dimethylamino)phenyl]-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP03	J1	358-360	359-361

Int.	Structure	Name	SM	method	MW	Mes
HP08		ethyl 4-chloro-3-isopropyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	AMP28	H3 Specific example	267-269	268-270
HP09		ethyl 4-chloro-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP08, 1765-93-1	I4	361-363	362-364
HP10		4-chloro-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP02	J1	327-329	328-330
HP11		4-chloro-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP05	J1	333-335	334-336

Int.	Structure	Name	SM	method	MW	Mes
HP12		methyl 4-chloro-1-cyclohexyl-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	AMP23	Specific example	335-337	336-338
HP13		ethyl 4-chloro-3-methyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	1131-18-6	Specific example	315-317	316-318
HP14		ethyl 3-cyclobutyl-1-[(2,4-dimethoxyphenyl)methyl]-4-(trifluoromethylsulfonyloxy)pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP15	Specific example	543	544

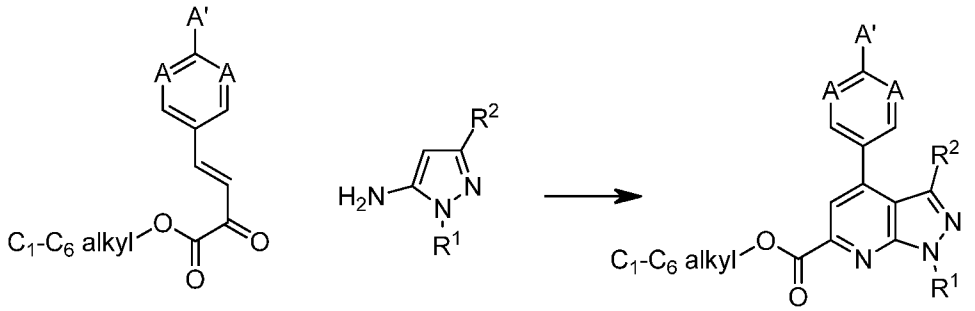
Int.	Structure	Name	SM	method	MW	Mes
HP15		ethyl 3-cyclobutyl-1-[(2,4-dimethoxyphenyl)methyl]-4-hydroxy-pyrazolo[3,4-*b*]pyridine-6-carboxylate	AMP36	H3 (steps 1 & 2 only)[1]	411	412
HP16		4-chloro-3-isopropyl-1-(*m*-tolyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP01	J1	329-331	330-332
HP19		methyl 4-chloro-3-cyclobutyl-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	AMP93	Specific example	359-361	360-362

Int.	Structure	Name	SM	method	MW	Mes
HP20		ethyl 1-*tert*-butyl-3-cyclobutyl-4-[(trifluoromethanesulfonyl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	AMP94	Specific example	449	450
HP25		methyl 4-chloro-3-cyclobutyl-1-cyclohexyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	AMP35	Specific example	347	348
HP26		4-chloro-3-cyclobutyl-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP19	J1	345	346

[1]Step 2 performed in Dowtherm™ at 160 °C for 48 h.

Method I1-I34: Synthesis of esters

Method I1: Cyclization of alkylidene pyruvates and aminopyrazoles



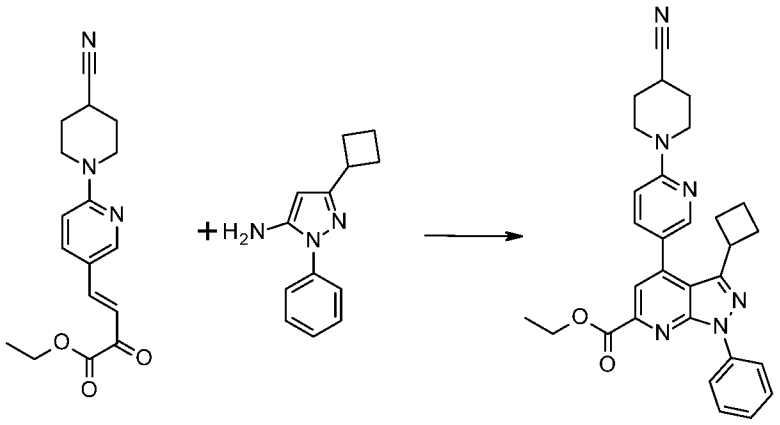
A is either N or CH

A' is either R^e or L^1-G^{3C} as described in the Summary

[00461] The alkylidene pyruvate (1 to 1.5 equiv) and the aminopyrazole (1 to 1.5 equiv) in acetic acid or DMF are stirred under air at temperatures ranging from RT to reflux for 1 h to several days. Alternatively, the reaction mixture is heated under microwave irradiation at 150 °C for 20 minutes to 2 h followed either by stirring under air in an opened flask at temperatures ranging from RT to 90 °C for 1 h to several days or by removal of the solvent in vacuo, dilution of the residue in ethanol and stirring at reflux for 1 h to several days. Then volatiles are removed in vacuo to afford the titled compound which is used as such or alternatively worked up by dilution with an organic solvent, washed successively with a basic aqueous solution and brine, dried over sodium sulfate, filtered and concentrated in vacuo and used as such or further purified either by precipitation, by preparative HPLC or by flash chromatography on silica gel.

[00462] Alternatively, the alkylidene pyruvate (1 equiv) and the aminopyrazole (1 equiv) in *N*-methylpyrrolidone can be heated at 80 to 100 °C over 8 to 24 hours. Next, the reaction mixture is cooled down to room temperature and a base such as Cs_2CO_3 (2-6 equiv) is added. The resulting mixture is stirred open to the air until full oxidation is observed.

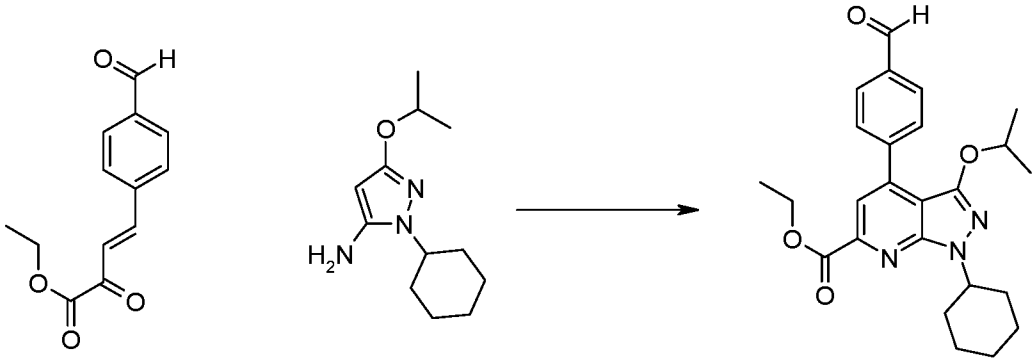
Illustrative synthesis of E018: 4-(4-Cyano-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-5'-yl)-3-cyclobutyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxylic acid ethyl ester



[00463] The alkylidene pyruvate ALP09 (47.1 g, 150.5 mmol) and the aminopyrazole AMP29 (30 g, 140.7 mmol) were dissolved in acetic acid (240 mL) in an opened round bottom flask equipped with a condenser. The solution was heated at 80 °C for 40 hours and then left cooling

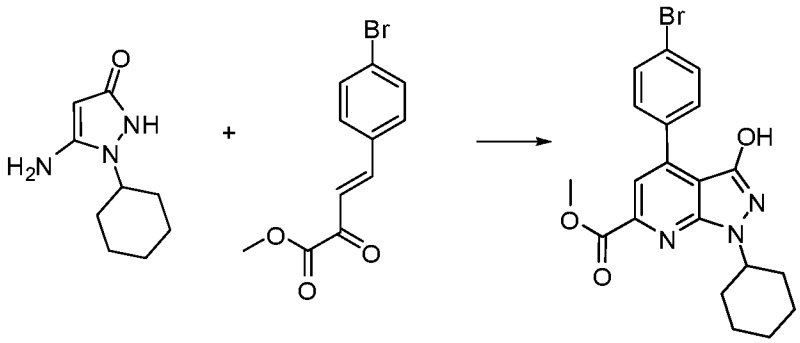
down to RT. The mixture was concentrated under reduced pressure, and the crude residue was diluted with DCM (400 mL). The organic phase was washed successively with a saturated aqueous solution of Na_2CO_3 and a saturated aqueous solution of NaCl, dried over sodium sulfate, filtered and concentrated in vacuo. The crude sample was purified by flash column chromatography eluting with dichloromethane/ethyl acetate. The solid was stirred for 10 minutes in methanol, filtered and dried at 40 °C under reduced pressure to give the titled compound.

Illustrative synthesis of E425: ethyl 1-cyclohexyl-4-(4-formylphenyl)-3-[(propan-2-yl)oxy]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate



[00464] A solution of ALP36 (116 mg, 0.5 mmol) and AMP95 (112 mg, 0.5 mmol) in *N*-methylpyrrolidine (2 mL) was heated at 100 °C for 20 hours in a sealed tube. The volatiles were removed in vacuo, and the residue was purified by flash chromatography on silica gel eluted with ethyl acetate/*n*-heptane (0/1 to 1/0) to give the titled compound.

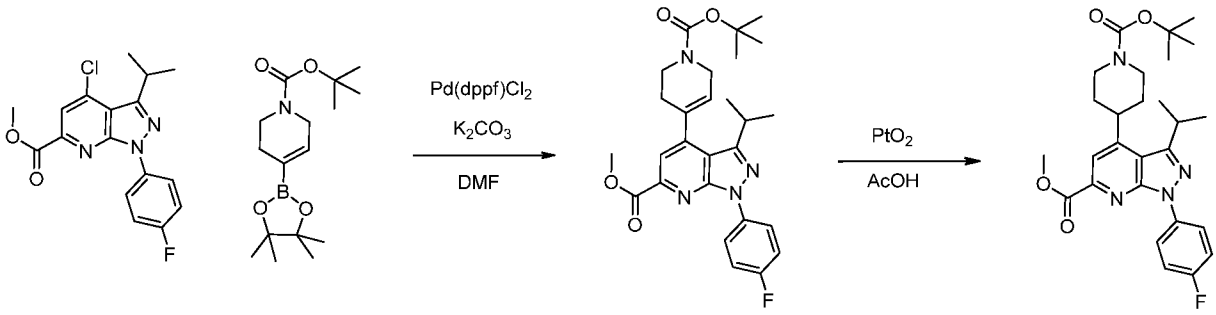
Illustrative synthesis of E503: methyl 4-(4-bromophenyl)-1-cyclohexyl-3-hydroxy-1H-pyrazolo[3,4-b]pyridine-6-carboxylate



[00465] 5-Amino-1-cyclohexyl-1*H*-pyrazol-3-ol ([436088-86-7], 5.54 g, 30.5 mmol,) and (*E*)-methyl-4-(4-bromophenyl)-2-oxobut-3-enoate ([608128-34-3], 8.22 g, 30.5 mmol,) in NMP (60 mL,) were heated overnight at 90 °C. Next, the reaction mixture was cooled down to room temperature and Cs_2CO_3 (30 g, 91.6 mmol) was added. The resulting mixture was stirred open to the air until full oxidation to the titled compound was observed. The obtained solution was used as such for alkylation.

Method I2: Suzuki coupling

Illustrative synthesis of E197 and E198: methyl 4-(1-tert-butoxycarbonyl-4-piperidyl)-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-b]pyridine-6-carboxylate and methyl 4-(1-tert-butoxycarbonyl-3,6-dihydro-2H-pyridin-4-yl)-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-b]pyridine-6-carboxylate



[00466] *Step 1: methyl 4-(1-tert-butoxycarbonyl-3,6-dihydro-2H-pyridin-4-yl)-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-b]pyridine-6-carboxylate E198*

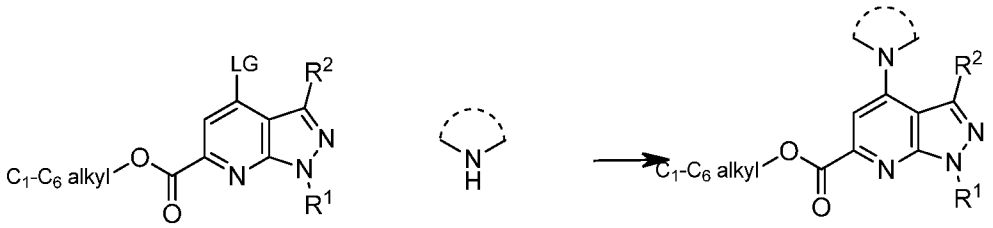
[00467] A suspension of methyl 4-chloro-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate (HP05, 2.0 g, 5.75 mmol, 1.0 equiv), *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,6-dihydro-2*H*-pyridine-1-carboxylate (CAS 286961-14-6, 3.6 g, 11.5 mmol, 2.0 equiv), K_2CO_3 (2.4 g, 17.25 mmol, 3.0 equiv)and $Pd(dppf)Cl_2$ (CAS : 72287-26-4, 939 mg, 1.15 mmol, 0.2 equiv) in anhydrous DMF (15 mL) was degassed with nitrogen at room temperature for 2 minutes. The reaction mixture was heated at reflux overnight. The mixture was cooled to RT, and the mixture was poured into 150 mL of water and diluted with ethyl acetate. The two phases were separated, and the aqueous phase was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and

concentrated. The crude residue was purified by silica gel chromatography (heptane/ethyl acetate: 100/0 to 80/20) to give E198.

[00468] *Step 2: methyl 4-(1-tert-butoxycarbonyl-4-piperidyl)-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-b]pyridine-6-carboxylate*

[00469] A suspension of E198 (2.44 g, 4.93 mmol, 1.0 equiv) and platinum(IV) oxide (CAS 1314-15-4, 1.2 g) in AcOH was stirred at RT under hydrogen atmosphere (balloon) overnight. Then the reaction mixture was filtered over Celpure® P65. Solids were washed with ethyl acetate, and the filtrate was concentrated in vacuo. The crude residue was purified by silica gel chromatography (heptane/ethyl acetate: 100/0 to 80/20) to give the title compound.

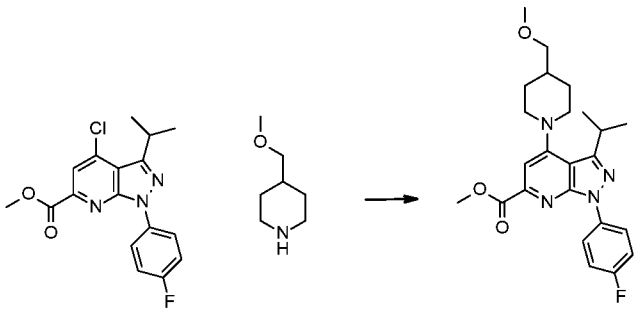
Method I3: Nucleophilic substitutions of amines



LG = Cl, OTf

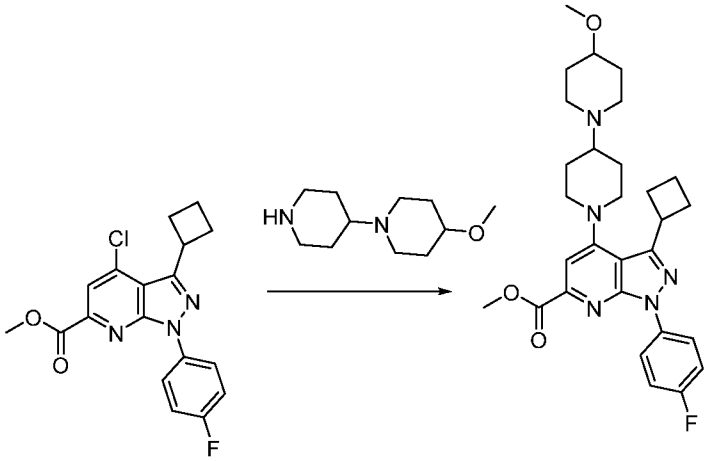
[00470] A mixture of the chloride or triflate pyrazolopyridine intermediate (1.0 equiv), the amine as free base or hydrochloride salt (from 1 to 10 equiv) and DIPEA (from 1 to 15 equiv) in anhydrous acetonitrile and DMSO in a sealed tube or a round bottom flask is heated at a temperature ranging from 50 to 130 °C for 1 h to several days (up to 8 days). The reaction mixture is cooled to RT, and volatiles are removed in vacuo. The resulting residue is either purified by precipitation or by flash chromatography on silica gel to afford the titled compound or alternatively partitioned between either dichloromethane or ethyl acetate and water. The two phases are then separated, and the aqueous phase is extracted with either ethyl acetate or dichloromethane. The combined organic phases are washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo and the resulting crude mixture is either used as such or purified by flash chromatography on silica gel to afford the titled compound.

Illustrative synthesis of E092: methyl 1-(4-fluorophenyl)-3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]pyrazolo[3,4-b]pyridine-6-carboxylate



[00471] A mixture of HP05 (6.71g, 19.29 mmol, 1.0 equiv), 4-(methoxymethyl)piperidine hydrochloride (CAS 916317-00-5, 6.39g, 38.58 mmol, 2 equiv) and DIPEA (10.1 mL, 57.88 mmol, 3 equiv) in anhydrous DMSO (65 mL) was heated at 100 °C for 20 h. The reaction mixture was cooled to RT, partitioned between ethyl acetate (300 mL) and a mixture of water and a saturated solution of NaCl 1:1 (300 mL). The two phases were separated, and the aqueous phase was extracted with ethyl acetate (150 mL). The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The crude mixture was purified by flash chromatography on silica gel eluting with *n*-heptane/ethyl acetate to afford the titled compound.

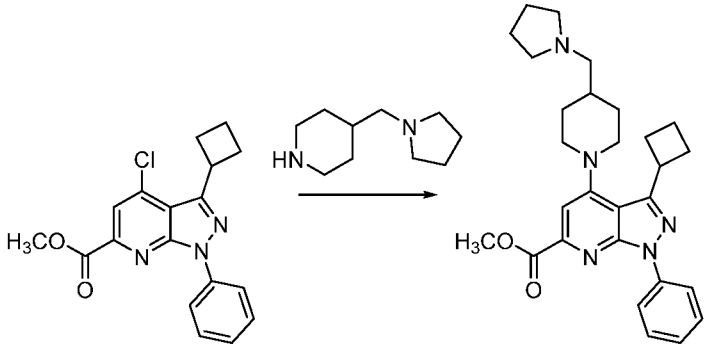
Illustrative synthesis of E356: methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(4-methoxy-1-piperidyl)-1-piperidyl]pyrazolo[3,4-b]pyridine-6-carboxylate



[00472] To a solution of HP19 (8.11 gram, 22.6 mmol) in dry *N*-methylpyrrolidinone (100 mL) was added 4-methoxy-1,4'-bipiperidine (5.37 gram, 27.1 mmol, AMI10) and diisopropylethylamine (9.42 mL, 54.2 mmol). The reaction mixture was stirred at 100 °C for 24 hours and then cooled down to ambient temperature and diluted with water. A suspension

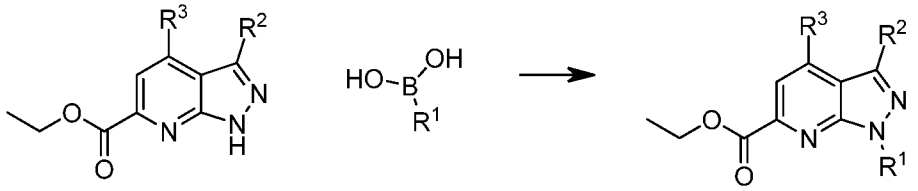
formed upon cooling at 0 °C. The suspension was filtered, and the obtained precipitate was washed with water. After drying, the titled compound was obtained.

*Illustrative synthesis of E357: methyl 3-cyclobutyl-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate*



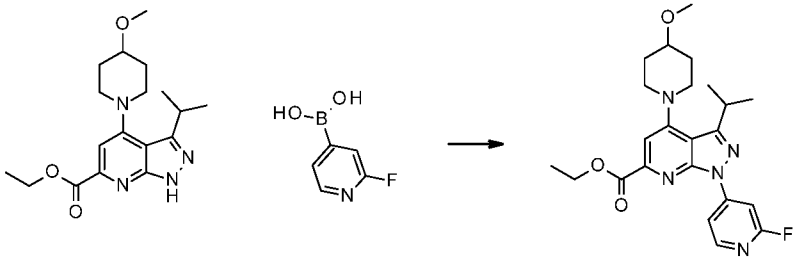
[00473] Methyl 4-chloro-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate (15 g, 43.9 mmol, HP02) and 4-(pyrrolidin-1-ylmethyl)piperidine (13.29 g, 79 mmol) were dissolved in a mixture of *N*-ethyl-*N*-isopropylpropan-2-amine (45.9 mL, 263 mmol) and *N*-methylpyrrolidinone (90 mL). The resulting solution was heated at 100 °C under nitrogen for two hours. After diluting with water (200 mL), the mixture was extracted with *tert*-butyl methyl ether (3 × 150 mL). The combined organic fractions were washed with 1 M aqueous NaOH (2 × 100 mL), water (2 × 50 mL), and saturated aqueous sodium chloride, then dried over sodium sulfate and concentrated under vacuum to approximately 100 mL followed by the addition of heptanes (200 mL). Volatiles were removed under vacuum, and the resulting thick slurry was stirred overnight at room temperature. The solid was collected by filtration, and then dried to constant weight under vacuum to give 18.39 g of the titled compound. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.39 – 8.31 (m, 2H), 7.51 (dd, J = 8.6, 7.4 Hz, 2H), 7.40 (s, 1H), 7.31 – 7.23 (m, 1H), 4.00 (m, 4H), 3.70 – 3.57 (m, 2H), 2.89 (td, J = 12.2, 2.4 Hz, 2H), 2.63 (dq, J = 11.7, 9.2 Hz, 2H), 2.56 – 2.49 (m, 4H), 2.47 – 2.38 (m, 4H), 2.05 (m, 4H), 1.86 – 1.78 (m, 4H), 1.73 (m, 1H), 1.53 (qd, J = 12.1, 3.7 Hz, 2H); LC/MS (APCI) *m/z* 474.6 $(M+H)^+$.

Method I4: Chan-Lam coupling



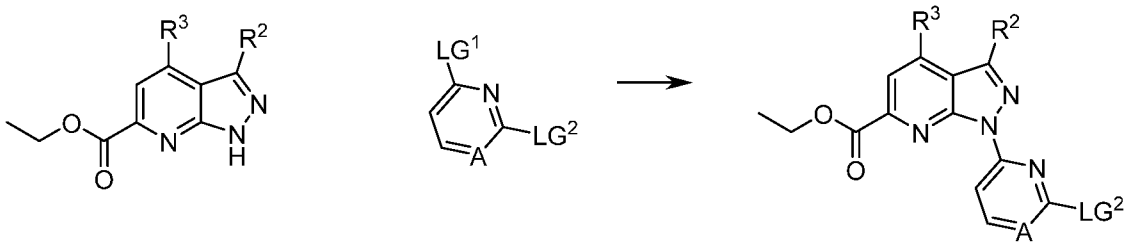
[00474] To a solution of ethyl 1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate intermediate (1.0 equiv) in dichloromethane at RT is added the aryl boronic acid (2.0 to 3.0 equiv), copper(II) acetate (CAS 142-71-2, 1.5 equiv) and pyridine (4.0 equiv). The reaction mixture is stirred at room temperature under air for 1 h to 48 h. Then the reaction mixture is filtered on a pad of diatomaceous earth. Solids are washed with dichloromethane, and the filtrate is concentrated in vacuo. The resulting residue is purified by flash chromatography on silica gel to afford the titled compound.

Illustrative synthesis of E111: ethyl 1-(2-fluoro-4-pyridyl)-3-isopropyl-4-(4-methoxy-1-piperidyl)pyrazolo[3,4-b]pyridine-6-carboxylate



[00475] To a solution of ethyl 3-isopropyl-4-(4-methoxy-1-piperidyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate E109 (70 mg, 0.20 mmol, 1.0 equiv) in dichloromethane (2 mL) at RT was added (2-fluoropyridin-4-yl)boronic acid (CAS: 401815-98-3, 56 mg, 0.40 mmol, 2.0 equiv), copper(II) acetate (CAS 142-71-2, 54 mg, 0.30 mmol, 1.5 equiv) and pyridine (64 µL, 0.80 mmol, 4.0 equiv). The reaction mixture was stirred at room temperature under air overnight. The reaction mixture was filtered on a pad of diatomaceous earth. Solids were washed with dichloromethane, and the filtrate was concentrated in vacuo. The resulting residue was purified by flash chromatography on silica gel (eluent system: heptane/ethyl acetate: 100/0 to 70/30) to give the titled compound.

Method I5: Nucleophilic substitution



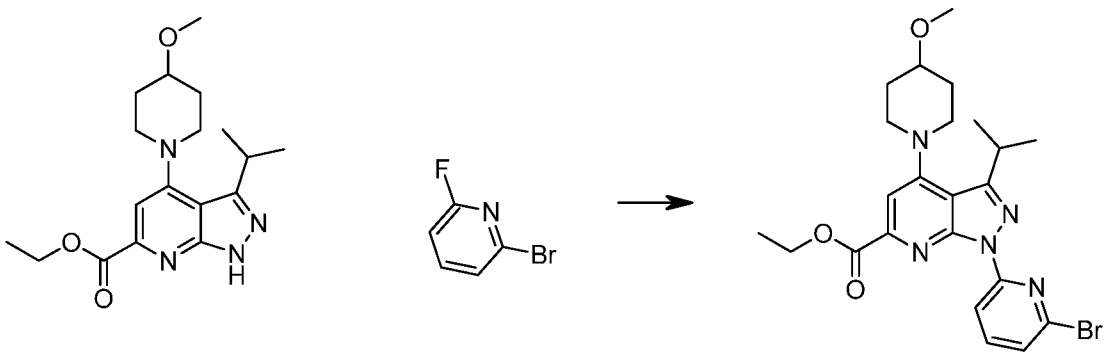
R^2 is isopropyl or cyclobutyl

A is CH or N

LG^1 and LG^2 are independently F, Cl or Br

[00476] To a solution of ethyl 3-substituted-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate intermediate (1.0 equiv) in anhydrous DMF or THF under nitrogen atmosphere at 0 °C is added sodium hydride (60% in mineral oil, from 1.2 equiv to 1.5equiv), and the mixture is stirred 5 minutes at 0 °C. Then an aromatic halide (2.0 equiv) is added, and the reaction mixture is warmed up to RT and stirred overnight. The reaction mixture is partitioned between water and ethyl acetate and acidified to pH 5 with AcOH. The two phases are separated. The organic phase is washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to afford the titled compound which is used as such or purified by flash chromatography on silica gel.

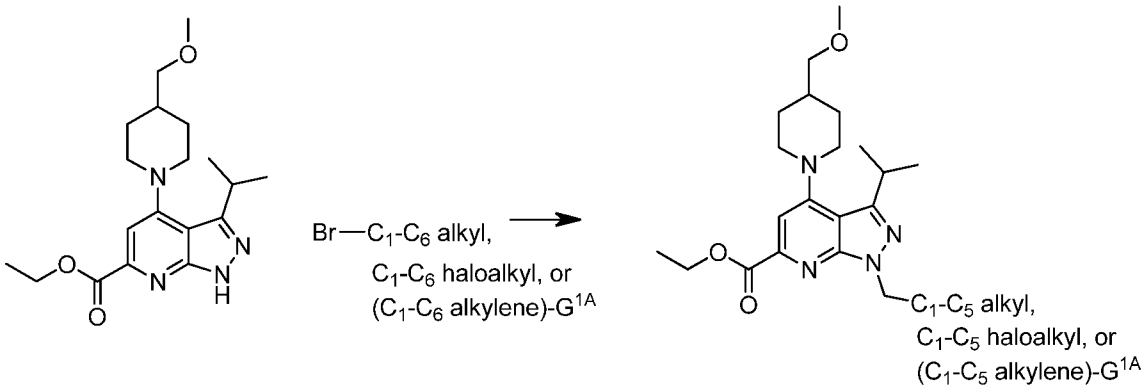
Illustrative synthesis of E133: ethyl 1-(6-bromo-2-pyridyl)-3-isopropyl-4-(4-methoxy-1-piperidyl)pyrazolo[3,4-b]pyridine-6-carboxylate



[00477] To a solution of ethyl 3-isopropyl-4-(4-methoxy-1-piperidyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate E109 (245 mg, 0.71 mmol, 1.0 equiv) in anhydrous DMF (3 mL) under nitrogen atmosphere at 0 °C was added sodium hydride (60% in mineral oil, 34 mg, 0.85 mmol, 1.2 equiv), and the mixture was stirred 5 minutes at 0 °C then 2-bromo-6-fluoropyridine (CAS 144100-07-2, 250 mg, 1.42 mmol, 2.0 equiv) was added, and the reaction mixture was warmed

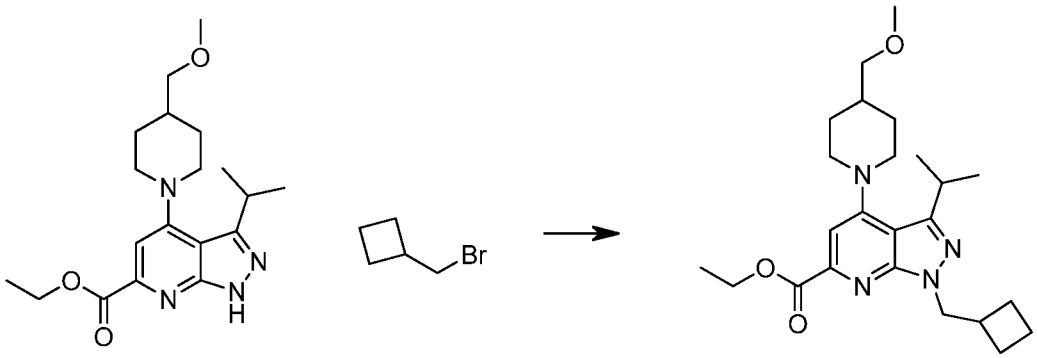
up to RT and stirred overnight. The reaction mixture was partitioned between water and ethyl acetate and acidified to pH 5 with AcOH. The two phases were separated. The organic phase was washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to afford the titled compound which was used as such.

Method I6: Alkylation



[00478] To a suspension of ethyl 3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate E148 (1.0 equiv) in anhydrous DMF under nitrogen atmosphere is added potassium carbonate (1.2 equiv), then alkyl bromide (1.1 equiv). The reaction mixture is stirred at room temperature overnight. Then cesium carbonate (1.2 equiv) and potassium iodide (0.1 equiv) are added, and the reaction mixture is stirred at room temperature for 24 h. The mixture is partitioned between water and ethyl acetate. The aqueous phase is extracted with ethyl acetate. The combined organic phases are washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The crude mixture is purified by flash chromatography on silica gel to afford the titled compound.

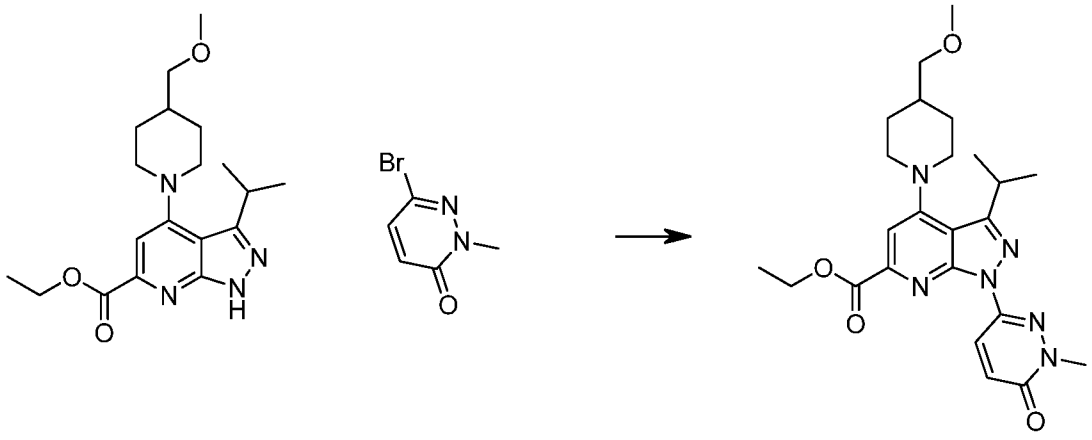
Illustrative synthesis of E154: ethyl 1-(cyclobutylmethyl)-3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]pyrazolo[3,4-b]pyridine-6-carboxylate



[00479] To a suspension of ethyl 3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate E148 (100 mg, 0.28 mmol, 1.0 equiv) in anhydrous DMF (2 mL) under nitrogen atmosphere was added potassium carbonate (47 mg, 0.34 mmol, 1.2 equiv) and then (bromomethyl)cyclobutane (CAS: 17247-58-4, 35 µL, 0.31 mmol, 1.1 equiv). The reaction mixture was stirred at room temperature overnight. Then cesium carbonate (111 mg, 0.34 mmol, 1.2 equiv) and potassium iodide (5 mg, 0.028 mmol, 0.1 equiv) were added, and the reaction mixture was stirred at room temperature for 24 h. The mixture was partitioned between water and ethyl acetate. The aqueous phase was extracted with ethyl acetate. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The crude mixture was purified by flash chromatography on silica gel (eluent system: heptane/ethyl acetate gradient from 100/0 to 75/25) to afford the titled compound.

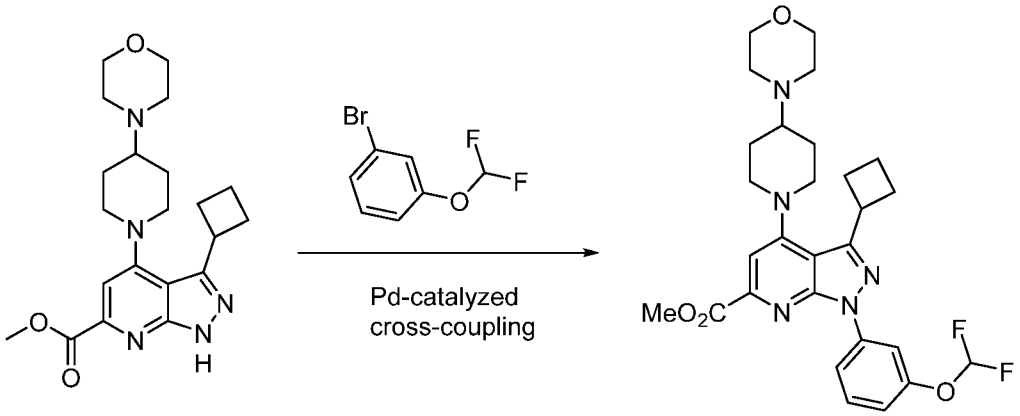
Method 17: Cross-coupling to pyrazole

Illustrative synthesis of E157: ethyl 3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]-1-(1-methyl-6-oxo-pyridazin-3-yl)pyrazolo[3,4-b]pyridine-6-carboxylate



[00480] A suspension of ethyl 3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate E148 (100 mg, 0.28 mmol, 1.0 equiv) in anhydrous toluene (1 mL) was degassed with nitrogen (bubbling) at room temperature for 5 minutes. Then to this suspension was added 6-bromo-2-methyl-pyridazin-3-one (CAS 1123169-25-4, 58 mg, 0.31 mmol, 1.1 equiv), cesium carbonate (365 mg, 1.12 mmol, 4.0 equiv), Xantphos (CAS 161265-03-8, 16 mg, 0.028 mmol, 0.1 equiv), and palladium(II) acetate (CAS 3375-31-3, 3 mg, 0.014 mmol, 0.05 equiv). The mixture was purged again with nitrogen at RT for 10 minutes, and then the mixture was stirred at reflux overnight. The reaction mixture was cooled down and concentrated in vacuo. The residue was partitioned between water and ethyl acetate. The aqueous phase was extracted with ethyl acetate. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The crude mixture was purified by flash chromatography on silica gel (eluent system: heptane/ethyl acetate gradient from 100/0 to 0/100) to afford the titled compound.

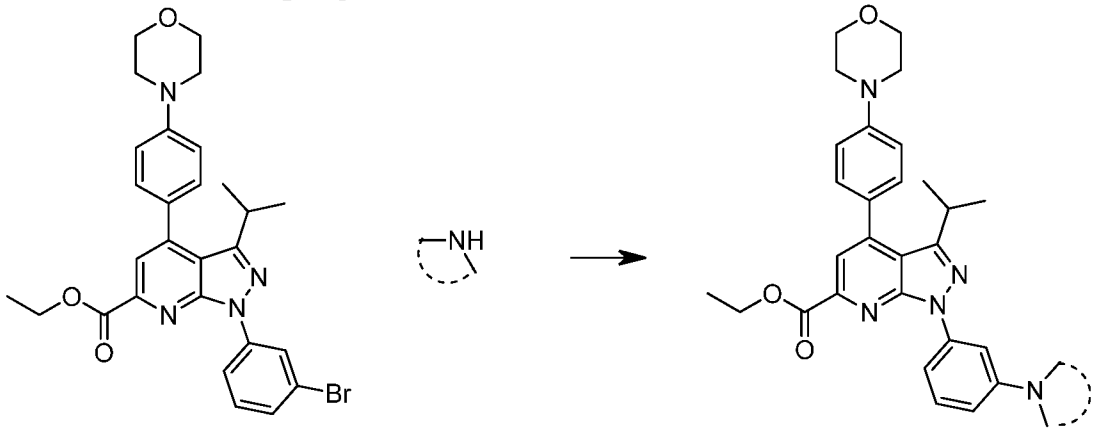
Illustrative synthesis of E510: methyl 3-cyclobutyl-1-[3-(difluoromethoxy)phenyl]-4-[4-(morpholin-4-yl)piperidin-1-yl]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate



[00481] A nitrogen-purged mixture of tris(dibenzylideneacetone)dipalladium(0) (0.0193 g, 0.021 mmol), and di-*tert*-butyl(2',4',6'-triisopropyl-3,4,5,6-tetramethyl-[1,1'-biphenyl]-2-yl)phosphine (0.0251 g, 0.052 mmol) in toluene (2.2 mL) was stirred for 20 minutes and then added to an nitrogen-purged mixture of methyl 3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate (0.1760 g, 0.441 mmol, E509), 1-bromo-3-(difluoromethoxy)benzene (0.1179 g, 0.529 mmol), and Cs_2CO_3 (0.2143 g, 0.658 mmol). The mixture was heated to 70 °C overnight, diluted with water, extracted with DCM (3 x 8 mL),

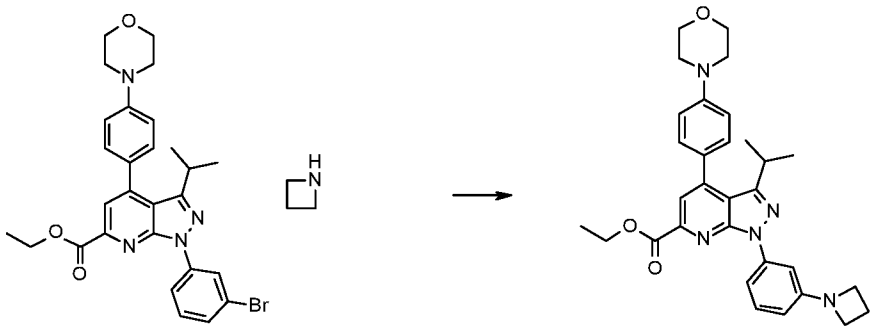
dried (Na_2SO_4), and concentrated. The residue was chromatographed on silica (30-60% EtOAc/DCM to 4% MeOH/DCM) and re-chromatographed (2.5-4% *i*PrOH/DCM) to give the titled compound. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.28 – 8.16 (m, 2H), 7.58 (t, J = 8.2 Hz, 1H), 7.51 – 7.03 (m, 3H), 3.95 (dq, J = 18.1, 9.8, 8.5 Hz, 1H), 3.88 (s, 3H), 3.63 – 3.48 (m, 6H), 2.91 (t, J = 11.9 Hz, 2H), 2.53 - 2.48 (m, 4H), 2.46 – 2.28 (m, 2H), 2.12 – 1.88 (m, 4H), 1.63 (td, J = 13.1, 12.6, 6.4 Hz, 2H).

Method I8: Buchwald coupling



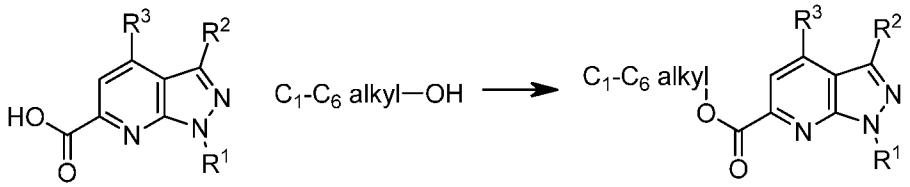
[00482] A suspension of ethyl 1-(3-bromophenyl)-3-isopropyl-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate E001 (1.0 equiv), XPhos Pd G1 (CAS 1028206-56-5, 0.1 equiv) and sodium *tert*-butoxide (CAS: 865-48-5, 1.3 equiv) in anhydrous toluene is degassed with argon (bubbling) at room temperature for 15 minutes. Amine (1.3 equiv) is added, and the mixture is purged with argon at RT for 2 minutes. The reaction mixture is stirred at 100 °C for 30 minutes to 24 h. The reaction mixture is concentrated in vacuo, and the residue is partitioned between water and dichloromethane and filtered on a pad of Celpure P65®. Solids were washed with dichloromethane and water, and the two phases of the filtrate are separated. The aqueous layer is extracted with dichloromethane. The combined organic phases are washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The titled compound is obtained from the crude mixture either by precipitation or by purification by flash chromatography on silica gel.

Illustrative synthesis of E002: ethyl 1-[3-(azetidin-1-yl)phenyl]-3-isopropyl-4-(4-morpholinophenyl)pyrazolo[3,4-b]pyridine-6-carboxylate



[00483] A suspension of ethyl 1-(3-bromophenyl)-3-isopropyl-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate E001 (60 mg, 0.115 mmol, 1.0 equiv), XPhos Pd G1 (CAS 1028206-56-5, 9 mg, 0.011 mmol, 0.1 equiv), and sodium *tert*-butoxide (CAS: 865-48-5, 14 mg, 0.149 mmol, 1.3 equiv) in anhydrous toluene (1.2 mL) was degassed with argon (bubbling) at room temperature for 15 minutes. Azetidine (13 µL, 0.149 mmol, 1.3 equiv) was added, and the mixture was purged with argon at RT for 2 minutes. The reaction mixture was stirred at 100 °C for 1 hour. The reaction mixture was concentrated in vacuo; the residue was partitioned between water and dichloromethane, and then was filtered on a pad of Celpure P65®. Solids were washed with dichloromethane and water, and the two phases of the filtrate were separated. The aqueous layer was extracted with dichloromethane. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (eluent system: dichloromethane/methanol gradient from 100/0 to 90/10). The obtained solid was suspended in ethanol, filtered, washed with diethyl ether and dried in vacuo to afford the titled compound.

Method I9: esterification

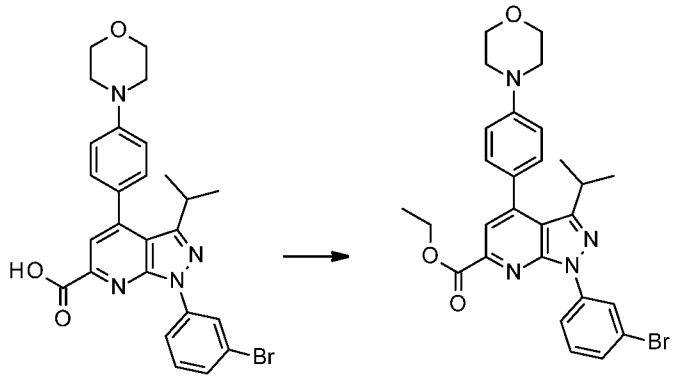


[00484] To the acid (1 equiv) in either ethanol or methanol at RT is added concentrated sulfuric acid (catalytic amount). The reaction mixture is refluxed for 1 h to several days (up to 8 days). Then the reaction mixture is cooled down to RT. The resulting suspension is filtered; the solid is washed with either ethanol or methanol and then dried in vacuo. The crude solid is

purified by flash chromatography on silica gel (eluent system: heptane/ethyl acetate) to give the titled compound.

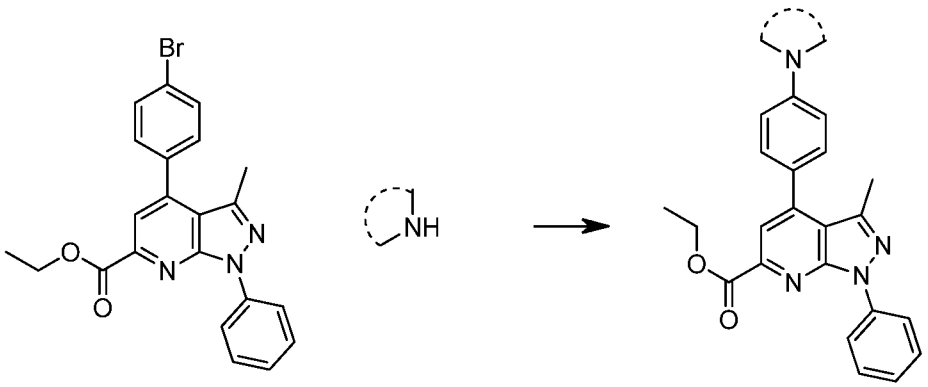
[00485] Alternatively, if no suspension is formed when cooling down the reaction mixture, the solvent is removed in vacuo. The resulting residue is taken up in dichloromethane and basified with a saturated solution of $NaHCO_3$. The two phases are separated, and the aqueous phase is extracted with dichloromethane. The combined organic phases are washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to afford the titled compound which is used as such or further purified by flash chromatography on silica gel.

Illustrative synthesis of: E001 ethyl 1-(3-bromophenyl)-3-isopropyl-4-(4-morpholinophenyl)pyrazolo[3,4-b]pyridine-6-carboxylate



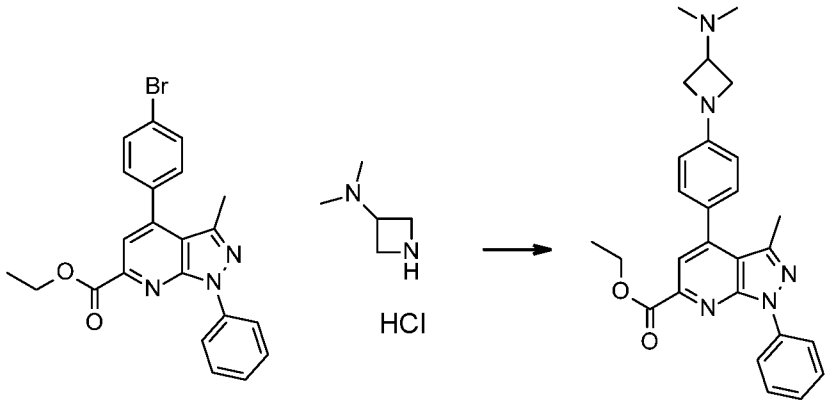
[00486] Concentrated sulfuric acid (0.23 mL) was added to a suspension of A242 (2.56 g, 4.9 mmol) in absolute ethanol (64 mL) at RT. The reaction mixture was refluxed for 5 hours. The reaction mixture was cooled down to RT, and the obtained suspension was filtered. The cake was washed with ethanol and dried in vacuo. The solid residue was purified by chromatography on silica gel (heptane/ethyl acetate 100/0 to 70/30) to give the titled compound.

Method I10: Buchwald coupling on the aryl linker



[00487] To the amine (from 1.3 to 2 equiv), E010 (1 equiv) and sodium *tert*-butoxide (CAS: 865-48-5, from 1.3 to 3 equiv) is added degassed anhydrous toluene. The reaction mixture is purged with argon, XPhos Pd G1 (CAS 1028206-56-5, 0.1 equiv) is added, and the mixture is purged again with argon. The reaction mixture is stirred at a temperature ranging from 90 °C to 110 °C for 1 h to 24 h. The reaction mixture is cooled down and filtered on a pad of diatomaceous earth. Solids are washed with organic solvents, and the combined filtrates are concentrated in vacuo. The resulting residue is purified by flash chromatography on silica gel to afford the titled compound.

Illustrative synthesis of E011: *ethyl 4-[4-[3-(dimethylamino)azetidin-1-yl]phenyl]-3-methyl-1-phenyl-pyrazolo[3,4-b]pyridine-6-carboxylate*

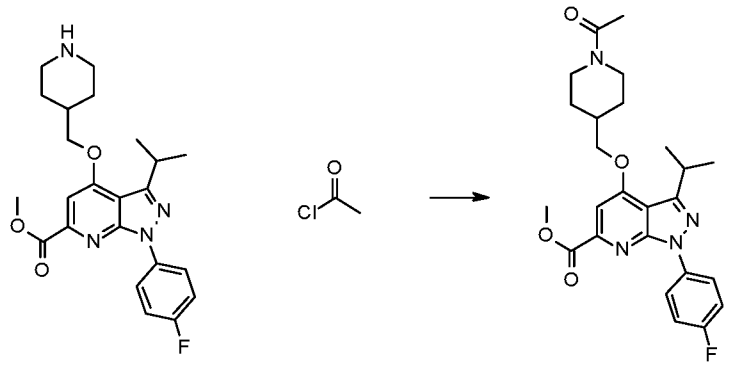


[00488] To *N,N*-dimethylazetidin-3-amine hydrochloride (CAS: 935670-07-8, 40 mg, 0.194 mmol, 1.3 equiv), E010 (100 mg, 0.23 mmol, 1 equiv) and sodium *tert*-butoxide (CAS: 865-48-5, 57 mg, 0.598 mmol, 2.6 equiv) was added degassed toluene (2 mL). The reaction mixture was purged with argon, XPhos Pd G1 (CAS 1028206-56-5, 17 mg, 0.023 mmol, 0.1 equiv) was added and the mixture was purged again with argon. The reaction mixture was stirred at 100 °C

for 1 hour. The reaction mixture was cooled down and filtered on a pad of diatomaceous earth. Solids were washed with toluene, ethyl acetate and dichloromethane, and the combined filtrates were concentrated in vacuo. The residue was purified by flash chromatography on silica gel (dichloromethane/methanol 98/2) to afford the titled compound.

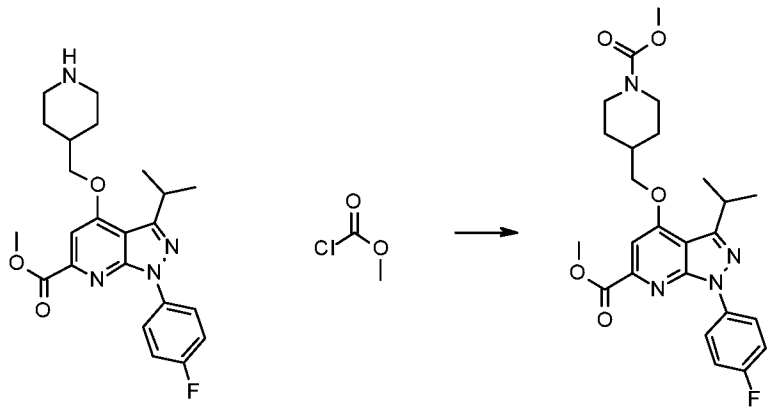
Method I11: acylation of amine

[00489] *Synthesis of E176: methyl 4-[(1-acetyl-4-piperidyl)methoxy]-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-b]pyridine-6-carboxylate*



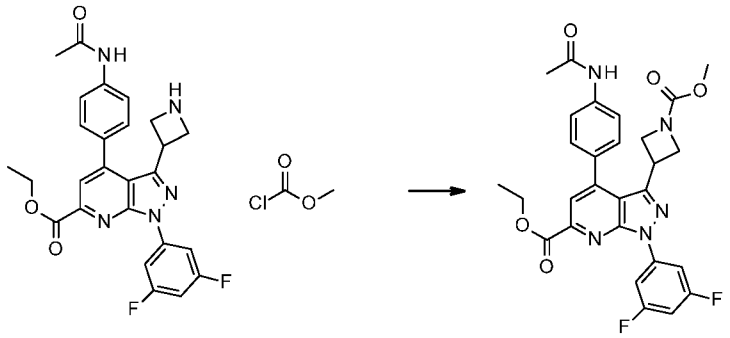
[00490] To E177 (0.1g, 0.23 mmol, 1 equiv) in anhydrous dichloromethane (2 mL) at RT was added acetyl chloride (CAS 75-36-5, 19 µL, 0.28 mmol, 1.2 equiv) followed by triethylamine (47 µL, 0.345 mmol, 1.5 equiv). The reaction mixture was stirred at RT for 2 h. The reaction mixture was diluted with dichloromethane and water. The two phases were separated, and the aqueous phase was extracted with dichloromethane. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting residue was purified by flash chromatography on silica gel (eluent system: heptane/ethyl acetate gradient from 100/0 to 0/100) to afford the titled compound.

[00491] *Synthesis of E178: methyl 1-(4-fluorophenyl)-3-isopropyl-4-[(1-methoxycarbonyl-4-piperidyl)methoxy]pyrazolo[3,4-b]pyridine-6-carboxylate*



To E177 (0.1g, 0.23 mmol, 1 equiv) in anhydrous dichloromethane (2 mL) at RT was added methyl chloroformate (CAS: 79-22-1, 19 µL, 0.28 mmol, 1.2 equiv) followed by triethylamine (47 µL, 0.345 mmol, 1.5 equiv). The reaction mixture was stirred at RT for 2 h. The reaction mixture was diluted with dichloromethane and water. The two phases were separated, and the aqueous phase was extracted with dichloromethane. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting residue was purified by flash chromatography on silica gel (eluent system: heptane/ethyl acetate gradient from 100/0 to 50/50) to afford the titled compound.

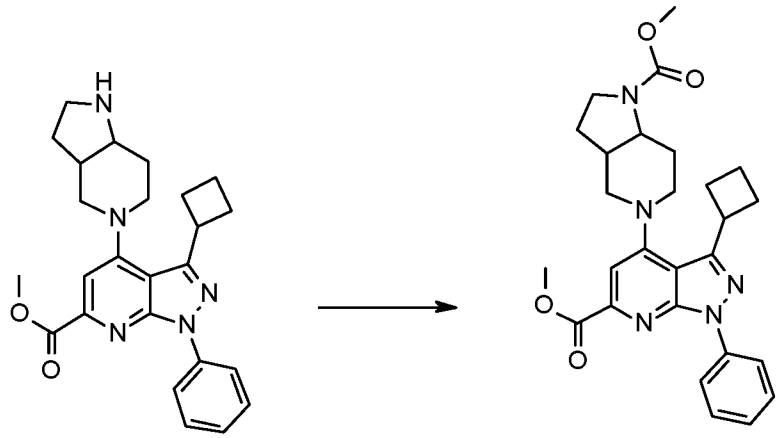
Synthesis of E042: ethyl 4-(4-acetamidophenyl)-1-(3,5-difluorophenyl)-3-(1-methoxycarbonylazetidin-3-yl)pyrazolo[3,4-b]pyridine-6-carboxylate



[00492] Diisopropylethylamine (0.045 mL, 0.26 mmol, 2.0 equiv) and 4-(dimethylamino)pyridine (CAS 1122-58-3, 3 mg, 0.026, 0.2 equiv) were added to a solution of E043 (65 mg, 0.13 mmol, 1 equiv) in dichloromethane (1 mL) at RT. The reaction mixture was cooled to 0 °C and methyl chloroformate (CAS: 79-22-1, 0.010 mL, 0.13 mmol, 1.0 equiv) was added. The reaction mixture was stirred at RT for 45 min then partitioned between

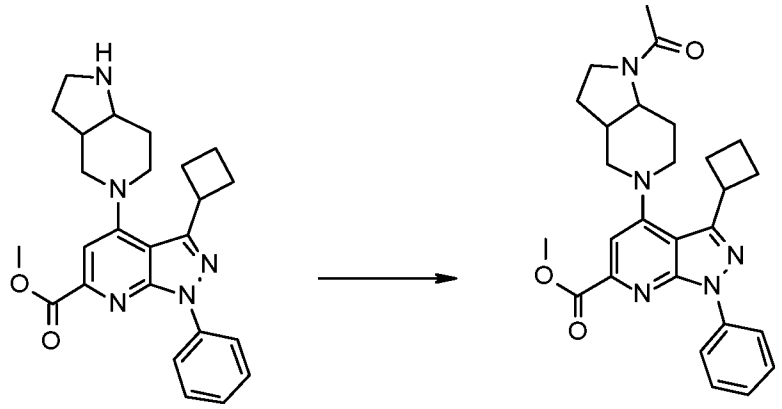
dichloromethane and water. The organic phase was separated, washed with water, dried over $MgSO_4$, filtered and concentrated. The residue was purified by silica gel chromatography (DCM/MeOH: 100/0 to 93/7) to give the titled compound.

Synthesis of E129: methyl 3-cyclobutyl-4-(1-methoxycarbonyl-3,3a,4,6,7,7a-hexahydro-2H-pyrrolo[3,2-c]pyridin-5-yl)-1-phenyl-pyrazolo[3,4-b]pyridine-6-carboxylate



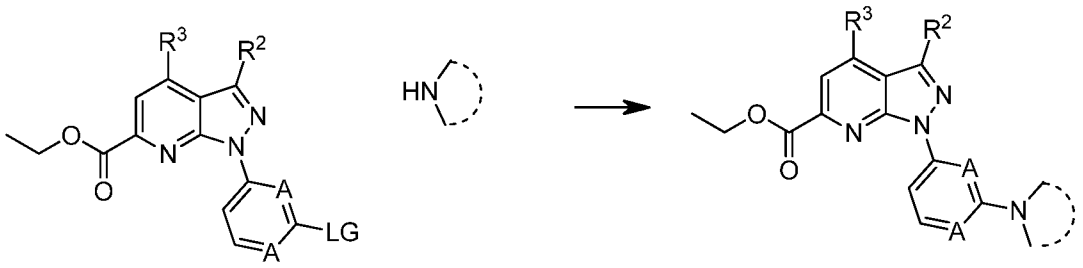
[00493] To E130 (31 mg, 0.073 mmol, 1 equiv) in anhydrous dichloromethane (0.5 mL) at 0 °C was added triethylamine (31 µL, 0.219 mmol, 3 equiv) followed by methyl chloroformate (CAS: 79-22-1, 7 µL, 0.088 mmol, 1.2 equiv). The reaction mixture was stirred at RT for 1.5 h. The reaction mixture was diluted with dichloromethane and water. The two phases were separated, and the aqueous phase was extracted with dichloromethane. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting residue was purified by flash chromatography on silica gel (eluent system: dichloromethane/methanol, gradient from 100/0 to 98/2) to afford the titled compound.

Synthesis of E132: methyl 4-(1-acetyl-3,3a,4,6,7,7a-hexahydro-2H-pyrrolo[3,2-c]pyridin-5-yl)-3-cyclobutyl-1-phenyl-pyrazolo[3,4-b]pyridine-6-carboxylate



[00494] To E130 (31 mg, 0.073 mmol, 1 equiv) in anhydrous dichloromethane (2 mL) at 0 °C was added (31 µL, 0.219 mmol, 3 equiv) followed by acetyl chloride (CAS 75-36-5, 5 µL, 0.088 mmol, 1.2 equiv). The reaction mixture was stirred at RT for 1.5 h. The reaction mixture was diluted with dichloromethane and water. The two phases were separated, and the aqueous phase was extracted with dichloromethane. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting residue was purified by flash chromatography on silica gel (eluent system: dichloromethane/methanol, gradient from 100/0 to 96/4) to afford the titled compound.

Method I12: Nucleophilic substitution

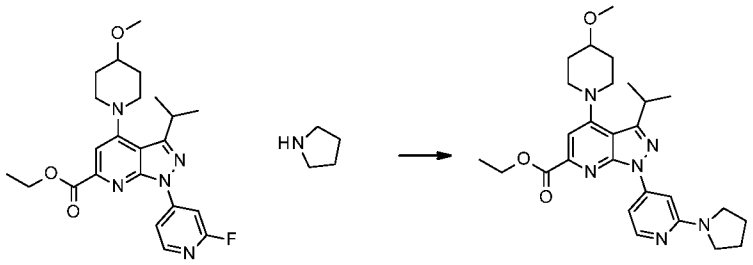


LG = F, Cl

A = CH, N

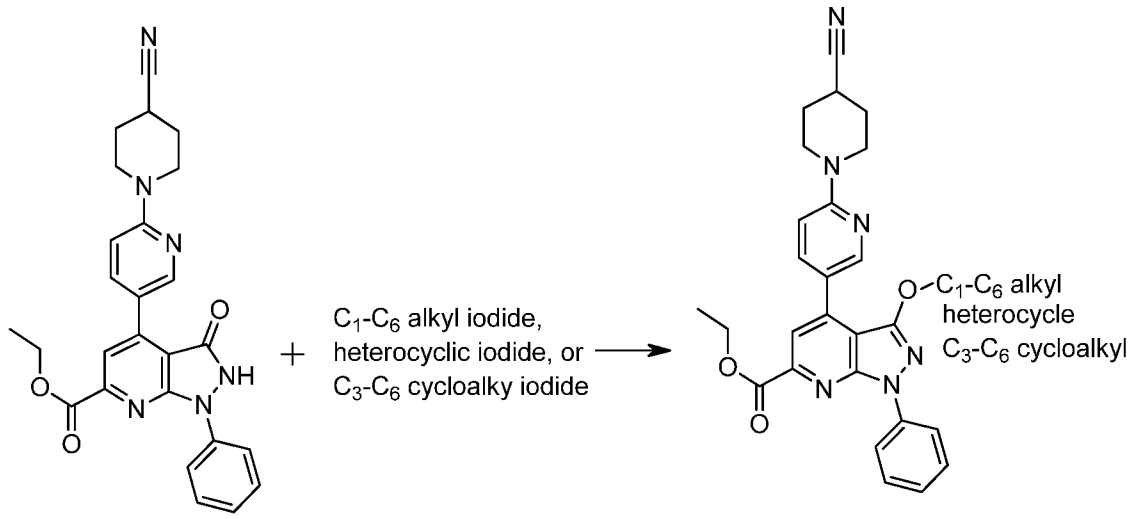
[00495] To a solution of the intermediate ester (1.0 equiv) in anhydrous DMSO, are added the amine (from 2.0 to 3.0 equiv) and K_2CO_3 (3.0 equiv). The reaction mixture is stirred at 100 °C overnight. The reaction mixture is cooled down to RT, poured into water and extracted with ethyl acetate. The combined organic layers are washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting residue is purified by silica gel chromatography to afford the titled compound.

Illustrative synthesis of E110: ethyl 3-isopropyl-4-(4-methoxy-1-piperidyl)-1-(2-pyrrolidin-1-yl-4-pyridyl)pyrazolo[3,4-b]pyridine-6-carboxylate



[00496] To a solution of ethyl 1-(2-fluoro-4-pyridyl)-3-isopropyl-4-(4-methoxy-1-piperidyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate E111 (50 mg, 0.11 mmol, 1.0 equiv) in anhydrous DMSO (1 mL), were added pyrrolidine (18 µL, 0.22 mmol, 2.0 equiv) and K_2CO_3 (46 mg, 0.33 mmol, 3.0 equiv). The reaction mixture was stirred at 100 °C overnight. The reaction mixture was cooled down to RT, poured into water and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The crude residue was purified by silica gel chromatography (heptane/ethyl acetate: 100/0 to 40/60) to afford the titled compound.

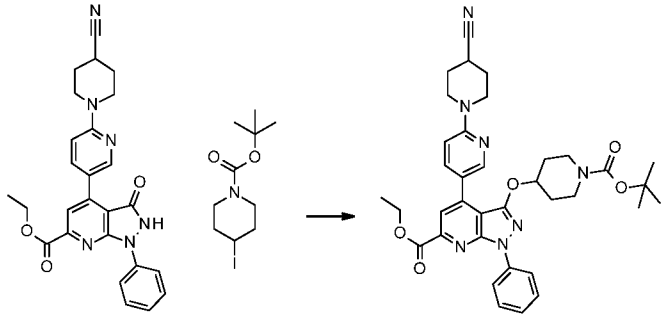
Method I13: O-alkylation of the pyrazole



[00497] Intermediate E153 (1.0 equiv), the alkyl iodide (from 3 to 5.7 equiv) and cesium carbonate (from 3 to 5.7 equiv) are charged in a sealed vial. NMP is added, and the vial is sealed. The reaction mixture is stirred at 130 °C for 1 hour. The reaction mixture is cooled

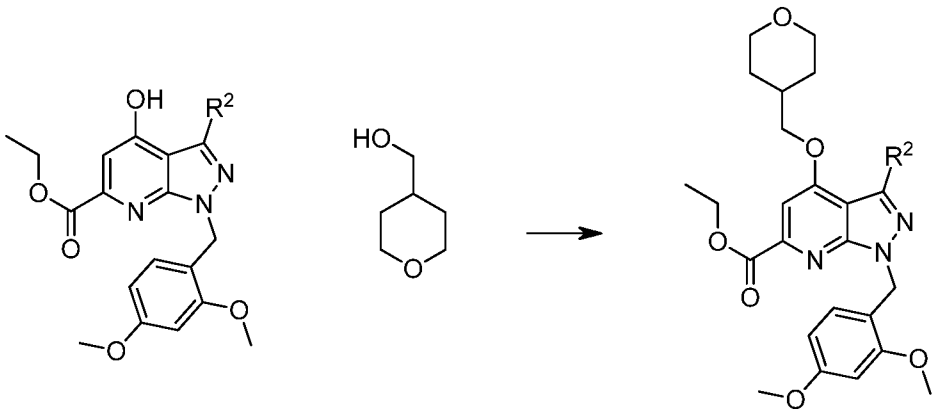
down to RT and partitioned between water and ethyl acetate. The phases are separated, and the aqueous phase is extracted with ethyl acetate. The combined organic phases are washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to afford the titled compound which is used as such or purified by flash chromatography on silica gel.

Illustrative synthesis of E152: ethyl 3-[(1-tert-butoxycarbonyl-4-piperidyl)oxy]-4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-1-phenyl-pyrazolo[3,4-b]pyridine-6-carboxylate



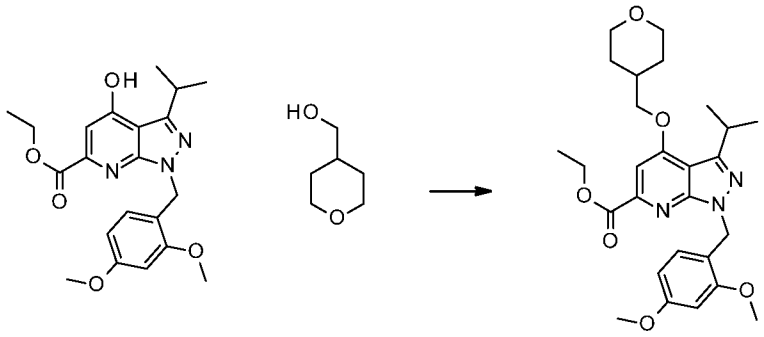
[00498] Intermediate E153 (110 mg, 0.23 mmol), *N*-Boc-4-iodo-piperidine (CAS: 301673-14-3, 410 mg, 1.32 mmol, 5.7 equiv) and cesium carbonate (430 mg, 1.32 mmol, 5.7 equiv) were charged in a sealed vial. NMP (2.9 mL) was added, and the vial was sealed. The reaction mixture was stirred at 130 °C for 1 hour. The reaction mixture was cooled down to RT and partitioned between water and ethyl acetate. The phases were separated, and the aqueous phase was extracted with ethyl acetate. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by silica gel chromatography (heptane/ethyl acetate: gradient from 100/0 to 2:1) to give the titled compound.

Method I14: Mitsunobu reaction



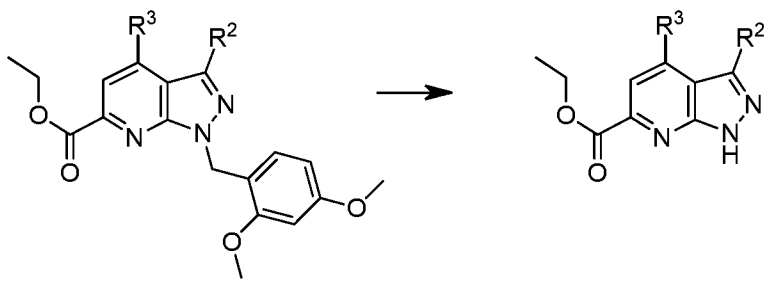
[00499] Diisopropyl azodicarboxylate (CAS: 2446-83-5, 0.606 mL, 3.075 mmol, 1.5 equiv) is added dropwise to a stirred solution of the intermediate phenol HP (1 equiv), tetrahydropyran-4-methanol (CAS: 14774-37-9, from 1.5 to 2.0 equiv) and triphenylphosphine (CAS: 603-35-0, 1.5 equiv) in tetrahydrofuran under nitrogen atmosphere. The reaction mixture is stirred at RT for 1 to 3 h. The solvent is removed under reduced pressure, and the resulting crude sample is purified by flash column chromatography on silica gel (eluent system: heptane/ethyl acetate) to yield the titled compound.

Illustrative synthesis of: E183 ethyl 1-[(2,4-dimethoxyphenyl)methyl]-3-isopropyl-4-(tetrahydropyran-4-ylmethoxy)pyrazolo[3,4-b]pyridine-6-carboxylate



[00500] Diisopropyl azodicarboxylate (CAS: 2446-83-5, 0.606 mL, 3.075 mmol, 1.5 equiv) was added dropwise to a stirred solution of HP06 (820 mg, 2.05 mmol), tetrahydropyran-4-methanol (CAS: 14774-37-9, 477 mg, 4.1 mmol, 2.0 equiv) and triphenylphosphine (CAS: 603-35-0, 806 mg, 3.075 mmol, 1.5 equiv) in tetrahydrofuran (20 mL) under nitrogen atmosphere. The reaction mixture was stirred at RT for 1 hour. The volatiles were removed under reduced pressure, and the crude sample was purified by flash column chromatography on silica gel eluting with *n*-heptane/ethyl acetate from 90/10 to 1/1 to yield the titled compound.

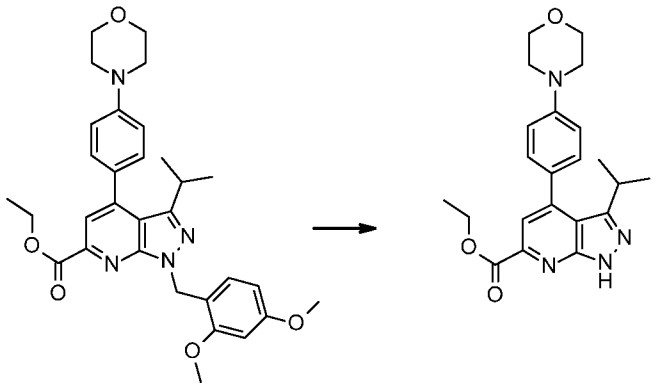
Method I15: dimethoxybenzyl group removal



[00501] Trifluoroacetic acid or a mixture of dichloromethane and trifluoroacetic acid is added to the (2,4-dimethoxyphenyl)methyl]pyrazolo[3,4-*b*]pyridine compound. The reaction mixture is stirred at RT for several hours. Then the titled compound is isolated by precipitation in diethyl ether directly from the reaction mixture or after removal of volatiles and is used as such or is taken up in dichloromethane and basified with a saturated solution of sodium hydrogencarbonate. The phases are separated and the aqueous phase is extracted with dichloromethane. The combined organic phases are washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to afford the titled compound which is used as such or further purified by silica gel chromatography.

[00502] Alternatively the reaction mixture is concentrated in vacuo. The residue is taken up in dichloromethane and basified with a saturated solution of sodium hydrogencarbonate. The phases are separated and the aqueous phase is extracted with dichloromethane. The combined organic phases are washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo which was used as such or purified by precipitation or by flash chromatography on silica gel.

Illustrative synthesis of compound E055: ethyl 3-isopropyl-4-(4-morpholinophenyl)-1H-pyrazolo[3,4-b]pyridine-6-carboxylate

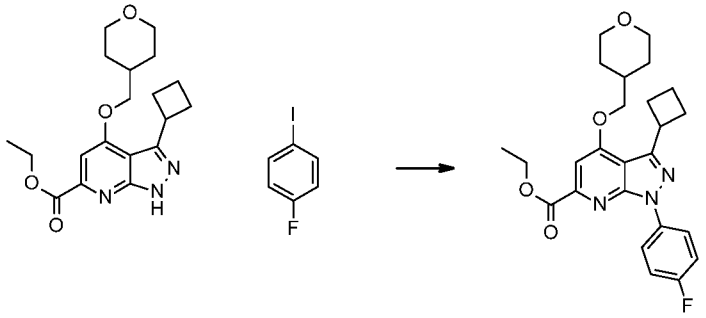


[00503] Trifluoroacetic acid (4.24 mL, 55.4 mmol, 71 equiv) was added to compound E056 (424 mg, 0.78 mmol). The reaction mixture was stirred at RT for 3 hours. Diethyl ether (20 mL) was added to the reaction mixture which was vigorously stirred for 5 minutes. The resulting suspension was filtered, and the cake was washed with diethyl ether. The solid was partitioned between dichloromethane and a saturated solution of sodium hydrogencarbonate and vigorously stirred. The suspension was filtered, and the solids were washed with dichloromethane. The two

phases of the filtrate were separated, and the aqueous phase was extracted with dichloromethane. The combined organic phases were dried over $MgSO_4$, filtered and concentrated in vacuo to yield the titled compound which was used without further purification.

Method I16: Ullmann coupling

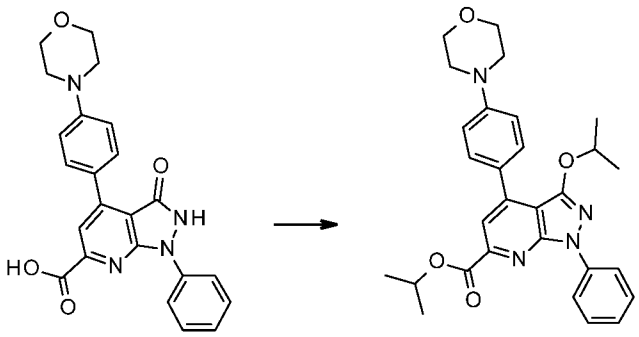
Synthesis of E171: ethyl 3-cyclobutyl-1-(4-fluorophenyl)-4-(tetrahydropyran-4-ylmethoxy)pyrazolo[3,4-b]pyridine-6-carboxylate



[00504] A degassed solution of *trans-N,N'*-dimethyl-1,2-cyclohexane (CAS: 67579-81-1, 0.002 mL, 0.01 mmol, 0.15 equiv) and 1-fluoro-4-iodobenzene (CAS: 352-34-1, 0.007 mL, 0.06 mmol, 0.7 equiv) in toluene (2 mL) was added to a mixture of E172 (30 mg, 0.08 mmol), K_3PO_4 (35 mg, 0.167 mmol, 2.0 equiv) and CuI (1 mg, 0.005 mmol, 0.07 equiv). The vial was sealed and the reaction mixture was stirred at 110 °C for 16 hours. The reaction mixture was cooled down to RT and partitioned between water and ethyl acetate. The organic phase was separated, dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by silica gel chromatography (dichloromethane/heptane/ethyl acetate: 100/0/0 to 0/70/30) to give the titled compound.

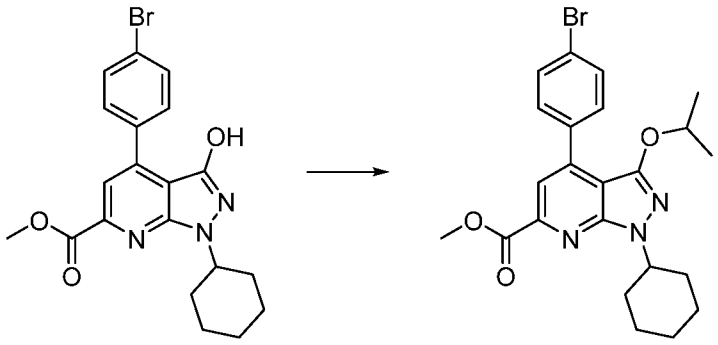
Method I17: O-Alkylation of pyrazole

Synthesis of compound E090: isopropyl 3-isopropoxy-4-(4-morpholinophenyl)-1-phenyl-pyrazolo[3,4-b]pyridine-6-carboxylate



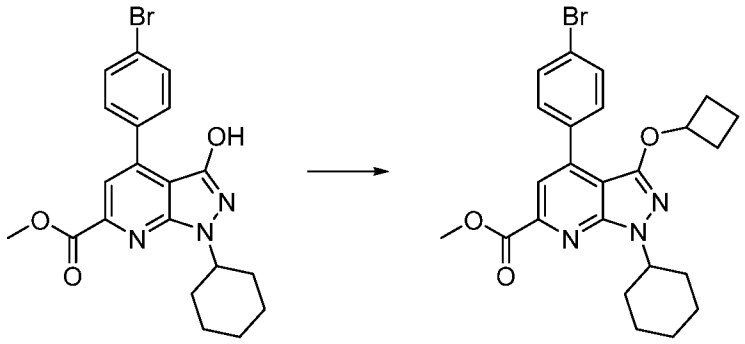
[00505] To a solution of A256 (330 mg, 0.79 mmol) and 2-iodopropane (CAS 75-30-9, 0.19 mL, 1.90 mmol, 2.4 equiv) in anhydrous NMP (4 mL) was added cesium carbonate (775 mg, 2.38 mmol, 3.0 equiv), and the reaction mixture was stirred at 130 °C for 16 hours. The reaction mixture was cooled down to RT and partitioned between dichloromethane and a saturated solution of sodium hydrogencarbonate. The organic phase was separated, washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by silica gel chromatography (petroleum ether/ethyl acetate: 80/20 to 70/30) to give the titled compound.

Synthesis of intermediate E504: methyl 4-(4-bromophenyl)-1-cyclohexyl-3-[(propan-2-yl)oxy]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate



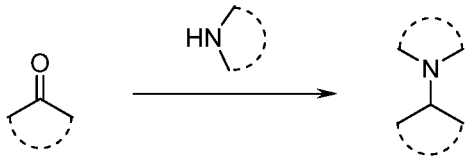
[00506] To a solution containing methyl 4-(4-bromophenyl)-1-cyclohexyl-3-hydroxy-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate (30.5 mmol, E503) was added isopropyl bromide ([75-26-3], 5.73 mL, 61.1 mmol) and cesium carbonate (2.70 g, 8.28 mmol), and the resulting mixture stirred under N_2 at 60 °C for 1 hour. The mixture was diluted with water and extracted with ethyl acetate. The organic phase was washed with brine (2x) and concentrated. The obtained residue was purified by column chromatography using a petroleum ether/EtOAc gradient (95/5 till 90/10) to afford the titled compound.

Synthesis of intermediate E505: methyl 4-(4-bromophenyl)-3-(cyclobutyloxy)-1-cyclohexyl-1H-pyrazolo[3,4-b]pyridine-6-carboxylate



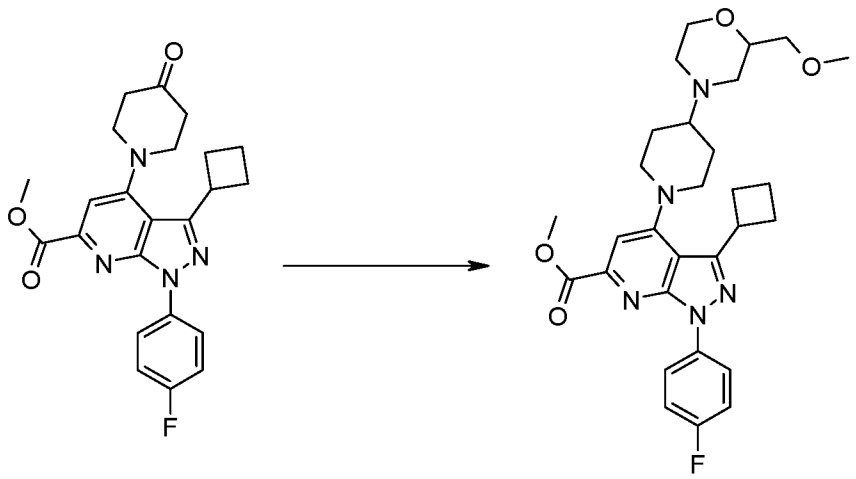
[00507] To a solution containing methyl 4-(4-bromophenyl)-1-cyclohexyl-3-hydroxy-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate (5.52 mmol, E503) was added cyclobutyl bromide ([4399-47-7], 1.04 mL, 11.0 mmol) and cesium carbonate (5.40 g, 11.0 mmol), and the resulting mixture stirred under N_2 at 60 °C for 1 hour. The mixture was diluted with water and extracted with ethyl acetate. The organic phase was washed with brine (2x) and concentrated. The obtained residue was purified by column chromatography using a petroleum ether/EtOAc gradient (95/5 till 90/10) to afford the titled compound.

Method I18: General method for reductive amination



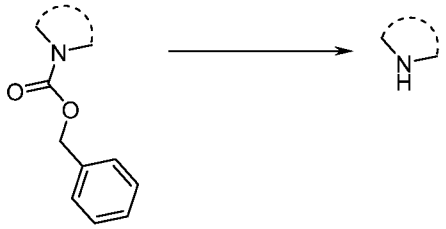
[00508] A suspension of ketone (1 eq), amine (1.5 to 3 eq) and triethylamine (1 to 2 eq) in dichloromethane is stirred at RT for 5 minutes. Acetic acid (1 to 2 eq) is added, and the stirring at RT is continued for 30 minutes. Sodium triacetoxyborohydride (1 to 3 eq) is then added, and the stirring is continued for 20 hours. The reaction mixture is diluted with dichloromethane and washed with a saturated aqueous solution of $NaHCO_3$. The organic phase is separated, dried over sodium sulfate and concentrated under reduced pressure. The crude sample is used as such or purified by flash column chromatography.

Illustrative synthesis of E354: methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[2-(methoxymethyl)morpholin-4-yl]piperidin-1-yl}-1H-pyrazolo[3,4-b]pyridine-6-carboxylate



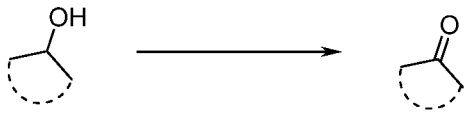
[00509] A suspension of E353 (0.1 g, 0.24 mmol), 2-(methoxymethyl)morpholine ([156121-15-2], 63 mg, 0.47 mmol) and triethylamine (33 µL, 0.24 mmol) in dichloromethane (2 mL) was stirred at RT for 5 minutes. Acetic acid (21 µL, 0.35 mmol) was added, and the stirring at RT was continued for 30 minutes. Sodium triacetoxyborohydride (76 mg, 0.35 mmol) was then added, and the stirring was continued for 20 hours. The reaction mixture was diluted with dichloromethane (3 mL) and washed with a saturated aqueous solution of $NaHCO_3$ (2 mL). The organic phase was separated using a phase separator and concentrated in vacuo to give the titled compound.

Method I19: General method for the reductive removal of benzyloxycarbonyl



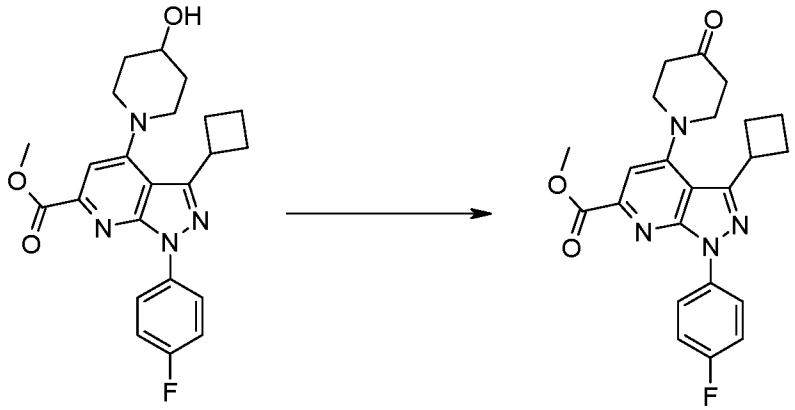
[00510] A solution of the benzyloxycarbonyl-protected amine (1 eq) in methanol is flushed with N_2. Next, 10% Pd/C (0.1 eq) is added and the mixture is put under hydrogen pressure with a balloon. After stirring overnight at ambient temperature, the mixture is filtered through diatomaceous earth, and the filtrate is concentrated. The residue is used as such or purified by flash column chromatography.

Method I23: General method for oxidation



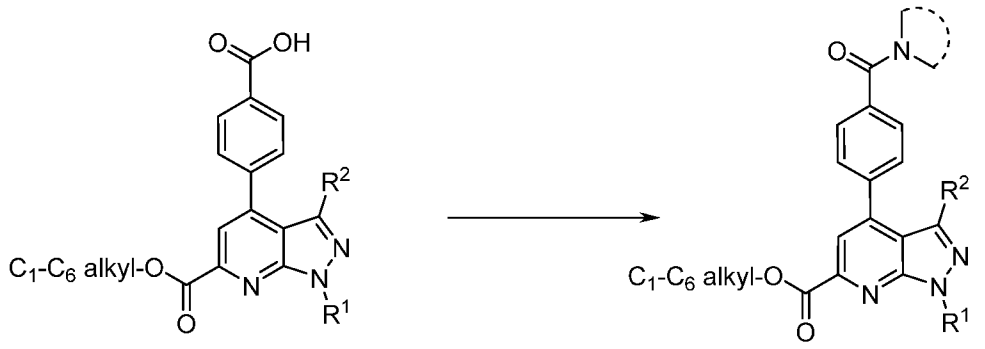
[00511] Dess Martin's periodinane (1 to 2 eq) is added at RT to a stirred solution of alcohol (1 eq) in dichloromethane. After 0.5 to 2 hours, the reaction mixture is diluted with dichloromethane. A solution of 20% $Na_2S_2O_3$ in water and a saturated aqueous solution of $NaHCO_3$ (1:1) is added and the stirring is continued for 30 minutes. The organic phase is separated, dried over sodium sulfate, filtered and concentrated under reduced pressure to give the titled compound. The compound can be used as such or purified by flash column chromatography.

Synthesis of compound E353: Methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-(4-oxopiperidin-1-yl)-1H-pyrazolo[3,4-b]pyridine-6-carboxylate



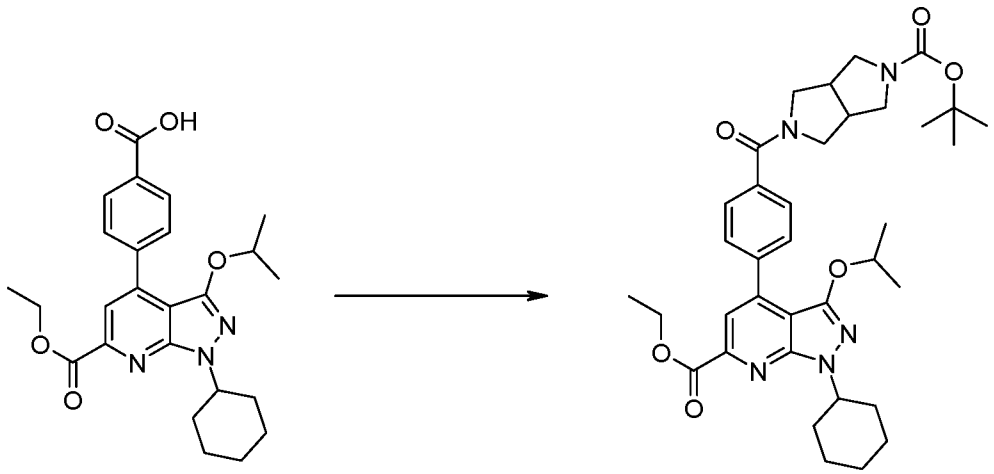
[00512] Dess-Martin periodinane (4 g, 9.4 mmol) was added at RT to a stirred solution of E352 (3.6 g, 8.6 mmol) in dichloromethane (40 mL). After 30 minutes, the reaction mixture was diluted with dichloromethane (50 mL). A solution of 20% aqueous $Na_2S_2O_3$ 20% and a saturated aqueous solution of $NaHCO_3$ (1:1, 50 mL) were added, and the stirring was continued for 30 minutes. The organic phase was separated, dried over sodium sulfate, filtered and concentrated under reduced pressure to give the titled compound.

Method I24: Coupling of amines



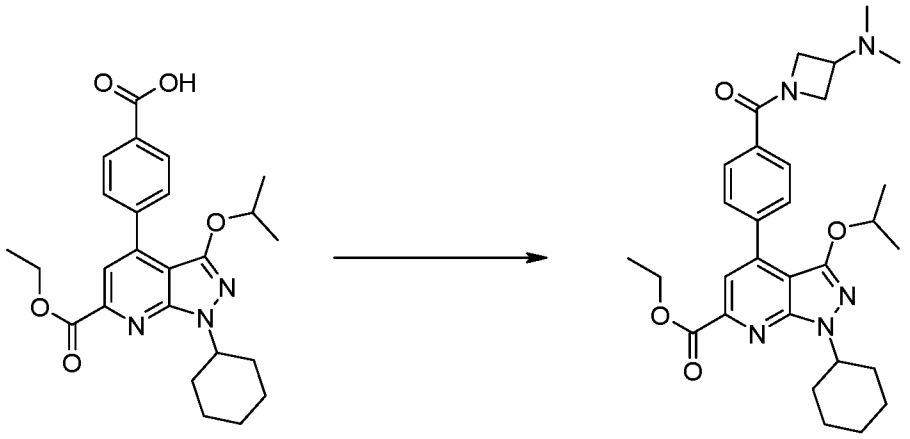
[00513] EDC•HCl ([25952-538], 1.2 equiv) is added at RT to a stirring solution of carboxylic acid (1 equiv), amine (4 equiv) and 4-(dimethylamino) pyridine ([1122-58-3], 2 equiv) in dichloromethane. The reaction mixture is stirred at RT for 20 hours. The solvent is evaporated under reduced pressure. The residue is purified flash column chromatography eluting with ethyl acetate/*n*-heptane and/or DCM/MeOH to yield the desired compound.

Illustrative Synthesis of E439: ethyl 4-{4-[5-(tert-butoxycarbonyl)hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carbonyl]phenyl}-1-cyclohexyl-3-[(propan-2-yl)oxy]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate



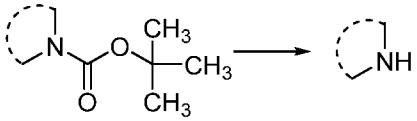
[00514] EDC•HCl ([25952-538], 18 mg, 74 µmol) was added at RT to a stirred solution of E438 (30 mg, 62 µmol), *tert*-butyl hexahydropyrrolo[3,4-*c*]pyrrole-2(1*H*)-carboxylate ([141449-85-6], 52 mg, 248 µmol) and 4-(dimethylamino) pyridine ([1122-58-3], 17 mg, 124 µmol) in dichloromethane (5 mL). The reaction mixture was stirred at RT for 20 hours. The mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography eluting with ethyl acetate/*n*-heptane to yield the titled compound.

Illustrative Synthesis of E441: ethyl 1-cyclohexyl-4-{4-[3-(dimethylamino)azetidine-1-carbonyl]phenyl}-3-[(propan-2-yl)oxy]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate



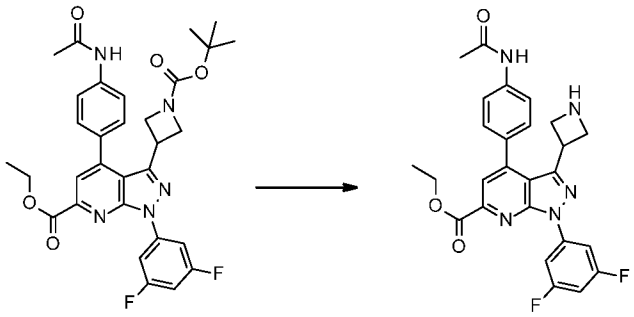
[00515] EDC•HCl ([25952-538], 24 mg, 125 µmol) was added at RT to a stirred solution of E438 (40 mg, 89 µmol), *N,N*-dimethylazetidin-3-amine hydrochloride ([935670-07-8], 49 mg, 358 µmol), triethylamine (50 µL, 358 µmol) and 4-(dimethylamino)pyridine ([1122-58-3], 24 mg, 196 µmol) in dichloromethane (15 mL). The reaction mixture was stirred at RT for 20 hours. The mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography eluting with ethyl acetate/DCM/MeOH (100/0/0 to 0/90/10) to yield the titled compound.

Method I25: tert-Butoxycarbonyl (Boc) deprotection



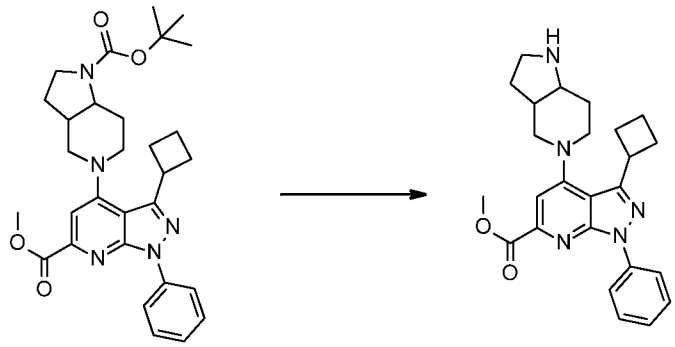
[00516] To a solution of the Boc-protected amine (1 eq) in dichloromethane at 0 °C, TFA (76-05-1, 5-20 eq) is added. The resulting mixture is stirred at room temperature until deprotection is complete. The mixture can be worked up by diluting the reaction mixture with DCM followed by washing with a saturated aqueous $NaHCO_3$ solution. The organic fraction is dried over sodium sulfate, filtered, and concentrated under reduced pressure to give the titled compound. Alternatively, the reaction mixture can be concentrated under reduced pressure, and the crude titled compound can be used as such without further purification.

Illustrative Synthesis of compound E043: ethyl 4-(4-acetamidophenyl)-3-(azetidin-3-yl)-1-(3,5-difluorophenyl)pyrazolo[3,4-b]pyridine-6-carboxylate



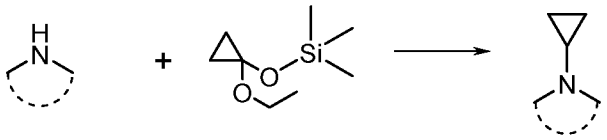
[00517] Trifluoroacetic acid (1.0 mL, 13.0 mmol, 33 equiv) was added at 0 °C to a solution of E044 (230 mg, 0.39 mmol) in dichloromethane (5.0 mL). The reaction mixture was stirred at RT for 1 hour. The reaction mixture was partitioned between dichloromethane and a saturated solution of sodium hydrogencarbonate. The organic phase was separated, dried over Na_2SO_4, filtered and concentrated to give the titled compound.

Illustrative Synthesis of compound E130: methyl 4-(1,2,3,3a,4,6,7,7a-octahydropyrrolo[3,2-c]pyridin-5-yl)-3-cyclobutyl-1-phenyl-pyrazolo[3,4-b]pyridine-6-carboxylate



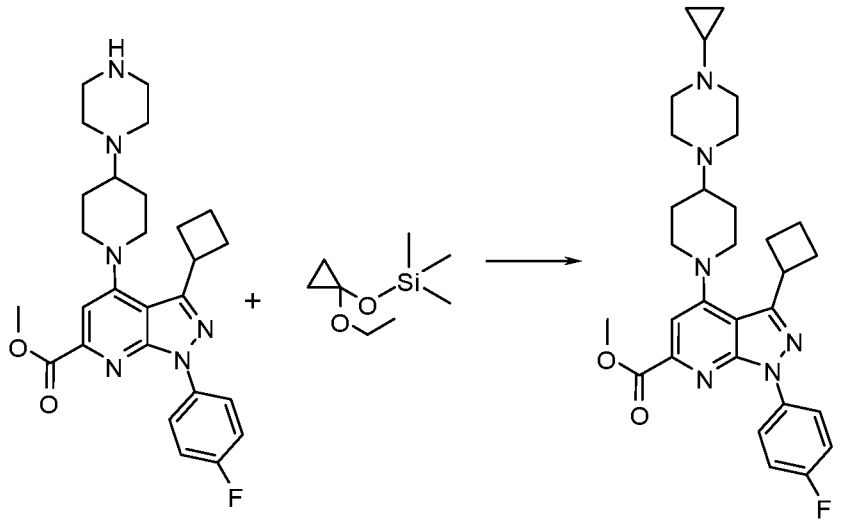
[00518] A solution of 4 M HCl in dioxane (0.245 mL, 0.98 mmol, 4.0 equiv) was added at RT to a solution of E131 (130 mg, 0.24 mmol) in dioxane (2.0 mL). The reaction mixture was stirred at RT for 16 hours. Additional 4 M HCl in dioxane (0.1 mL, 0.4 mmol, 1.7 equiv) was added, and the reaction mixture was stirred at RT for 48 hours. The reaction mixture was concentrated in vacuo and partitioned between dichloromethane and a saturated solution of sodium hydrogencarbonate. The organic phase was separated, dried over Na_2SO_4, filtered and concentrated in vacuo to give the titled compound.

Method I26: Reductive amination to install a cyclopropyl group



[00519] The amine (1 eq) is mixed with (1-ethoxycyclopropoxy)trimethylsilane ([27374-25-0], 2 eq), AcOH (1.6 eq) and $NaBH_3CN$ (1.5 eq) in a mixture of THF/MeOH (1/1). The resulting mixture is stirred overnight at 50 °C. After cooling the mixture down to room temperature, the reaction is quenched by the addition of water. Next, 1 M NaOH solution is added, and the mixture is stirred for another 15 minutes. After dilution with DCM, the organic layer is separated, dried and concentrated to give the titled compound.

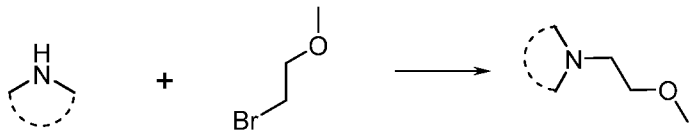
Illustrative synthesis of compound E465: methyl 3-cyclobutyl-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-1-(4-fluorophenyl)-1H-pyrazolo[3,4-b]pyridine-6-carboxylate



[00520] Methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(piperazin-1-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate (200 mg, 0.41 mmol, E498) was mixed with (1-ethoxycyclopropoxy)trimethylsilane ([27374-25-0], 163 µL, 0.81 mmol), AcOH (26 µL, 0.65 mmol) and sodium cyanoborohydride ([25895-60-7], 38 mg, 0.61 mmol) in a mixture of THF/MeOH (1/1, 1 mL). The resulting mixture was stirred overnight at 50 °C. After cooling the mixture down to room temperature, the reaction was quenched by the addition of water. Next, 1 M NaOH solution was added, and the mixture was stirred for another 15 minutes. After

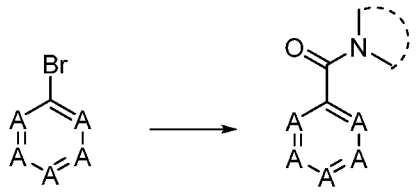
dilution with DCM, the organic layer was separated, dried and concentrated to give the titled compound.

Method I27: Alkylation amine



[00521] The amine (1 eq) is mixed with 1-bromo-2-methoxyethane ([6482-24-2], 1.1 eq) and K_2CO_3 (2 eq) in MeCN. The resulting mixture is heated at reflux overnight at 50 °C. After cooling down, the mixture is used as such in the next step.

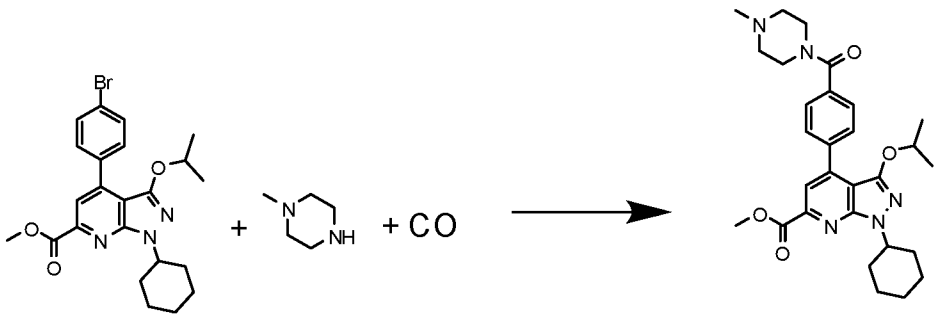
Method I28: Amino-carbonylation



A is CH or N

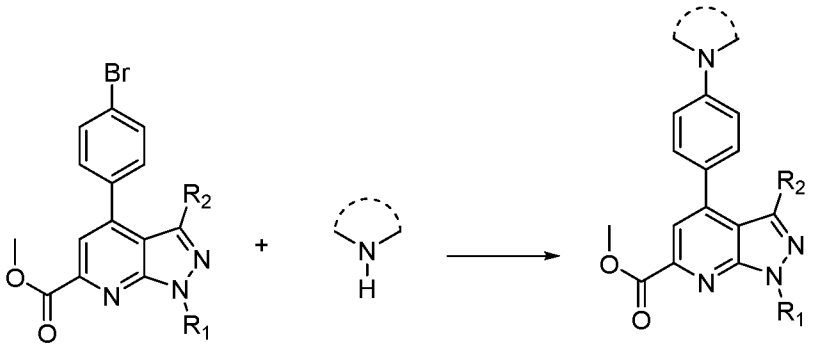
[00522] In a Parr reactor, the arylbromide (1 eq) is mixed with an amine (2 eq), Et_3N (4 eq) and Xantphos Pd G3 (0.03 eq) in dioxane. A CO pressure of 5 bars is applied and the mixture is heated at 100 °C overnight. Concentration gives a residue that is re-dissolved in DCM. Extraction with water gives an organic phase that is concentrated to give a residue that is used as such in the next step.

Illustrative synthesis of compound E474: methyl 1-cyclohexyl-4-[4-(4-methylpiperazine-1-carbonyl)phenyl]-3-[(propan-2-yl)oxy]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate



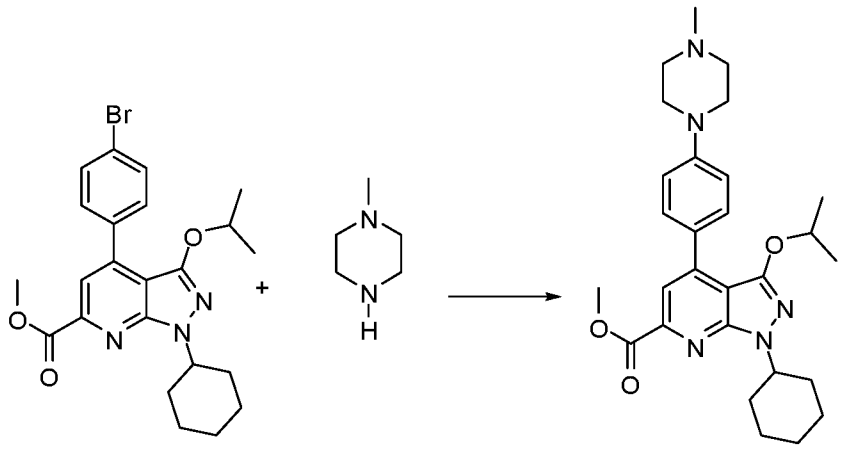
[00523] A Parr reactor was loaded with E504 (0.50 mmol, 250 mg), 1-methylpiperazine dihydrochloride ([34352-59-5], 1.0 mmol, 173 mg) and [(4,5-bis(diphenylphosphino)-9,9-dimethylxanthene)-2-(2′-amino-1,1′-biphenyl)]palladium(II) methanesulfonate] (0.015 mmol, 14 mg). The reactor was evacuated and back-filled with N_2, Et_3N (4.0 equiv, 2.0 mmol, 279 μL) and 1,4-dioxane (dry, 8 mL/mmol, 4 mL) were added, and the reaction mixture was heated to 100 °C under a CO atmosphere (5 bar) overnight. The reaction mixture was concentrated in vacuo, and the residue was partitioned between H_2O and dichloromethane. The organic phase was dried and concentrated in vacuo to give the titled compound which was used as such in the next step.

Method I29: Alternative Buchwald coupling on the aryl linker



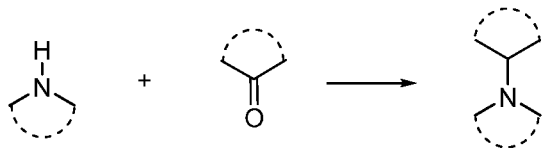
[00524] A tube is loaded with the arylbromide (1 eq). The amine (1.2 eq) is added together with (RuPhos) palladium(II) phenethylamine chloride (1:1 MTBE solvate, 0.1 eq), NaO*t*Bu (1.2 eq) in dioxane. The resulting suspension is put under a N_2 atmosphere and stirred at 100 °C. Next, the mixture is diluted with water and acidified with a 1 N citric acid solution till pH 3-4. Extraction with DCM gives the crude product that is either used as such or purified by chromatography. During this method, it is possible that partial hydrolysis of the ester to the corresponding acid occurs.

Illustrative synthesis of compound E502: methyl 1-cyclohexyl-4-[4-(4-methylpiperazin-1-yl)phenyl]-3-[(propan-2-yl)oxy]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate



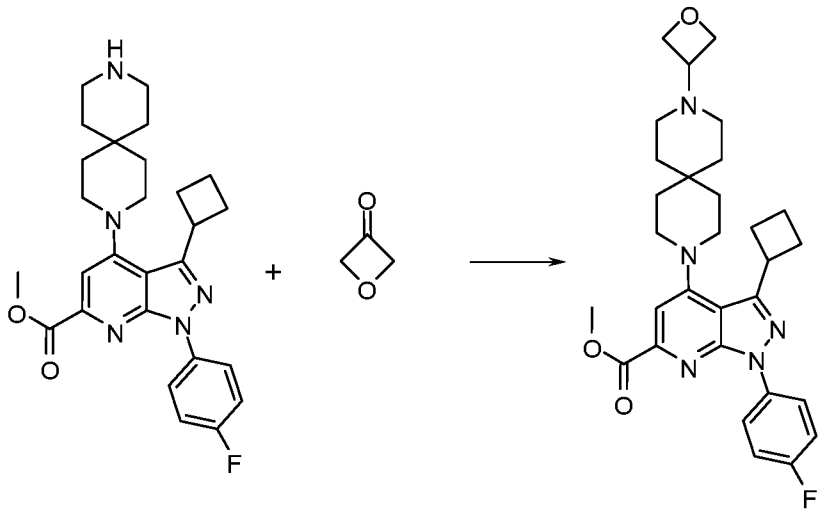
[00525] A tube was loaded with the E504 (100 mg, 0.21mmol). 1-Methylpiperazine ([109-01-3], 28µL, 0.25 mmol) was added together with (RuPhos) palladium(II) phenethylamine chloride (1:1 MTBE solvate, 17 mg, 0.02 mmol), and NaO*t*Bu (25 mg, 0.25 mmol) in dioxane (1 mL). The resulting suspension was put under a N_2 atmosphere and stirred at 100 °C. Next, the mixture was diluted with water and acidified with a 1 N citric acid solution till pH 3-4. Extraction with DCM gave the titled compound that was used as such. Partial hydrolysis of the ester to the corresponding acid was observed.

Method I30: Alternative reductive amination



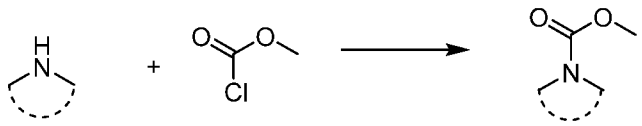
[00526] A solution of the amine (1 eq), the ketone (2 eq) and AcOH (1.5 eq) in DCM is cooled to 0 °C. Next, sodium triacetoxyborohydride ([56553-60-7], 2 eq) is added portionwise, and the reaction is stirred overnight at ambient temperature. Subsequently, the mixture is diluted with saturated $NaHCO_3$ solution and extracted with DCM. The organic phase is concentrated to give the alkylated amine that is used as such or purified by chromatography.

Illustrative example of compound E469: methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-[9-(oxetan-3-yl)-3,9-diazaspiro[5.5]undecan-3-yl]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate



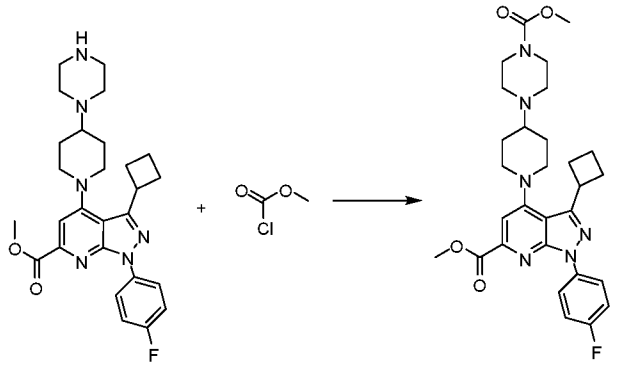
[00527] A solution of the methyl 3-cyclobutyl-4-(3,9-diazaspiro[5.5]undecan-3-yl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate (200 mg, 0.42 mmol, E500), 3-oxetanone ([6704-31-0], 54 µL, 0.84 mmol) and AcOH (36 µL) in DCM (3 mL) was cooled at 0 °C. Next, sodium triacetoxyborohydride ([56553-60-7], 178 mg, 0.84 mmol) was added portion wise and the reaction was stirred overnight at ambient temperature. Subsequently, the mixture was diluted with sat. $NaHCO_3$ solution and extracted with DCM. The organic phase was evaporated to give the titled compound.

Method I31: Carbamate synthesis



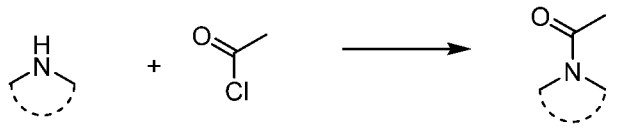
[00528] To a solution of the amine (1 eq) in DCM is added trimethylamine (2 eq) and then methyl chloroformate ([79-22-1], 2 eq). The mixture is stirred at RT overnight. Next, the reaction mixture is diluted with saturated $NaHCO_3$ solution and extracted with DCM. After concentration, the carbamate is obtained that is used as such or purified by chromatography.

Illustrative example of compound E486: methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[4-(methoxycarbonyl)piperazin-1-yl]piperidin-1-yl}-1H-pyrazolo[3,4-b]pyridine-6-carboxylate



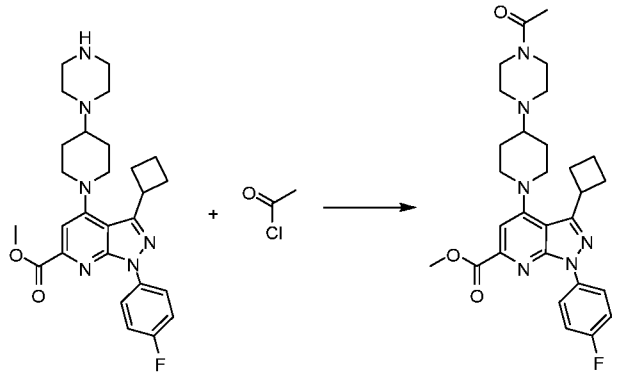
[00529] To a solution of the E498 (118 mg, 0.239 mmol) in DCM (1 mL) was added triethylamine (67 µL, 0.478 mmol) and then methyl chloroformate (37µL, 0.478 mmol). The mixture was stirred at RT overnight. Next, the reaction mixture was diluted with saturated $NaHCO_3$ solution and extracted with DCM. After concentration, the titled compound was obtained that was used as such.

Method I32: Amide synthesis using acetyl chloride



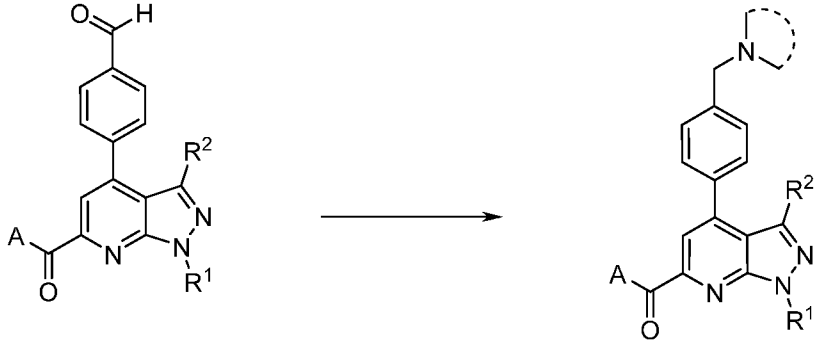
[00530] To a solution of the amine (1 eq) in DCM is added trimethylamine (2 eq) and then acetyl chloride ([75-36-5], 2 eq). The mixture is stirred at RT overnight. Next, the reaction mixture is diluted with saturated $NaHCO_3$ solution extracted with DCM. After concentration, the amide is obtained that is used as such or purified by chromatography.

Illustrative example of compound E487: methyl 4-[4-(4-acetylpiperazin-1-yl)piperidin-1-yl]-3-cyclobutyl-1-(4-fluorophenyl)-1H-pyrazolo[3,4-b]pyridine-6-carboxylate



[00531] To a solution of the E498 (118 mg, 0.239 mmol) in DCM (1 mL) was added triethylamine (67 µL, 0.478 mmol) and then acetyl chloride ([75-36-5], 0.478 mmol). The mixture was stirred at RT overnight. Next, the reaction was diluted with saturated $NaHCO_3$ solution and extracted with DCM. After concentration, the titled compound was obtained that was used as such.

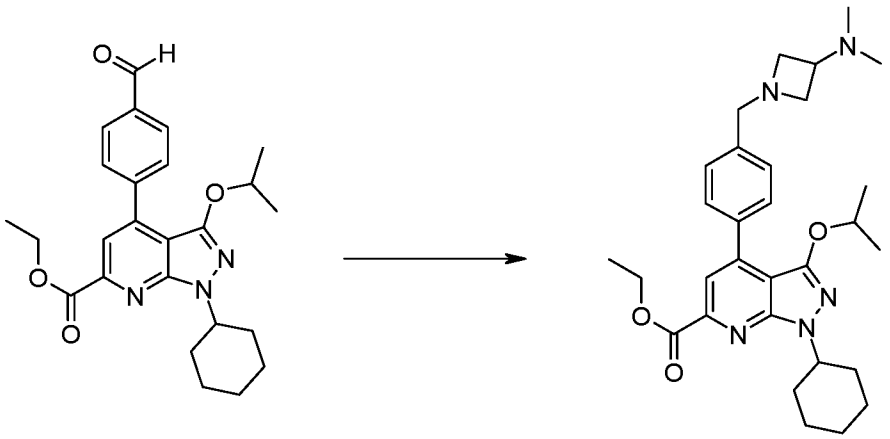
Method I34: Reductive amination on aldehydes



A is -O-C_1-C_6 alkyl or -$NHS(O)_2R^5$

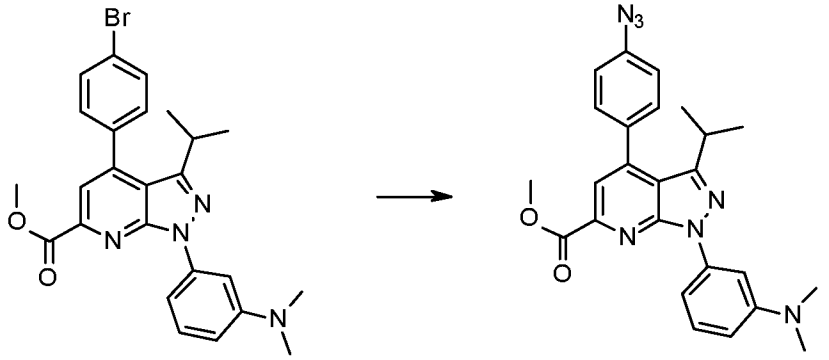
[00532] A suspension of amine hydrochloride or free base (1 to 2 equiv) and triethylamine (from 1 to 2 equiv) in 1,2-dichloroethane is stirred at RT for 10 minutes. Aldehyde (1 equiv), sodium triacetoxyborohydride (2 equiv), and acetic acid (0.6 to 4 equiv) are successively added, and the stirring at RT is continued for 20 hours. Starting reagents can be added until full conversion is observed. The reaction mixture is diluted with DCM, washed with a saturated aqueous solution of $NaHCO_3$ and/or a saturated aqueous solution of NH_4Cl and a phosphate buffer (pH 6.2). The organic phase is dried over sodium sulfate and concentrated under reduced pressure. The residue is used as such or purified by flash column chromatography to yield the reductively aminated compound.

Illustrative synthesis of E426: ethyl 1-cyclohexyl-4-(4-{[3-(dimethylamino)azetidin-1-yl]methyl}phenyl)-3-[(propan-2-yl)oxy]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate



[00533] A suspension of 3-(dimethylamino)azetidine dihydrochloride ([124668-49-1], 17 mg, 124 µmol) and triethylamine (35 µL, 248 µmol) in 1,2-dichloroethane (2 mL) was stirred at RT for 10 minutes. Aldehyde E425 (54 mg, 124 µmol), sodium triacetoxyborohydride (53 mg, 248 µmol), and acetic acid (29 µL, 496 µmol) were successively added, and the stirring at RT was continued for 20 hours. The reaction mixture was diluted with DCM and washed with a saturated aqueous solution of $NaHCO_3$. The organic phase was separated, dried over sodium sulfate and concentrated under reduced pressure. The residue was used as such or purified by flash column chromatography eluted with ethyl acetate/*n*-heptane to yield the titled compound.

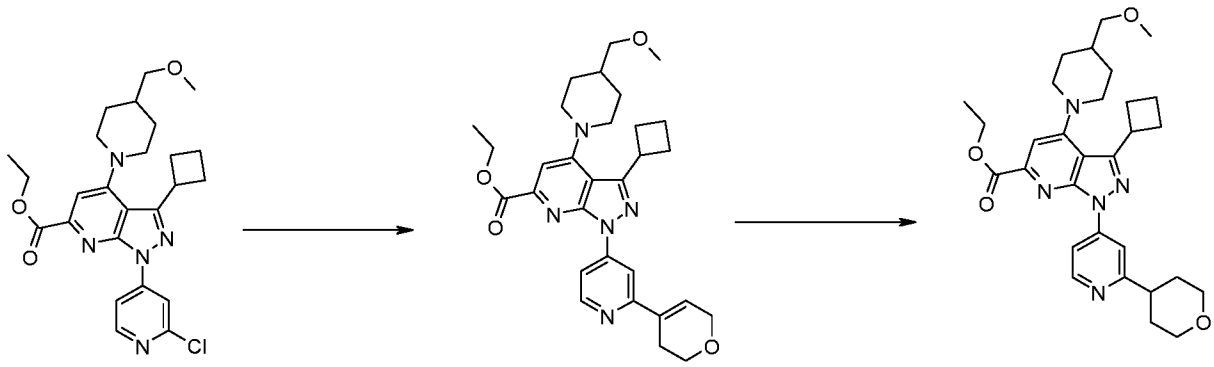
Synthesis of E199: methyl 4-(4-azidophenyl)-1-[3-(dimethylamino)phenyl]-3-isopropyl-pyrazolo[3,4-b]pyridine-6-carboxylate



[00534] Intermediate E074 (0.5g, 1.013 mmol, 1.0 equiv) and sodium azide (CAS 26628-22-8, 132 mg, 2.026 mmol, 2 equiv) were put in a sealed vial. A 2:1 mixture of ethanol and water (2 mL) was added, and the vial was purged with nitrogen. Then copper(I) iodide (CAS 7681-65-4, 20 mg, 0.101 mmol, 0.1 equiv), sodium ascorbate (CAS 134-03-2, 11 mg, 0.051 mmol, 0.05

equiv) and *N,N'*-dimethylethylenediamine (CAS 110-70-3, 45 µL, 0.405 mmol, 0.2 equiv) were added, and the vial was sealed. The reaction mixture was heated under microwave irradiation at 80 °C for 45 minutes. Volatiles were removed in vacuo. The resulting aqueous residue was diluted with ethyl acetate. The two phases were separated, and the aqueous phase was extracted with ethyl acetate. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to afford the titled compound which was used as such.

Synthesis of E390: ethyl 3-cyclobutyl-1-[2-(3,6-dihydro-2H-pyran-4-yl)pyridin-4-yl]-4-[4-(methoxymethyl)piperidin-1-yl]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate and E391: ethyl 3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-[2-(oxan-4-yl)pyridin-4-yl]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate



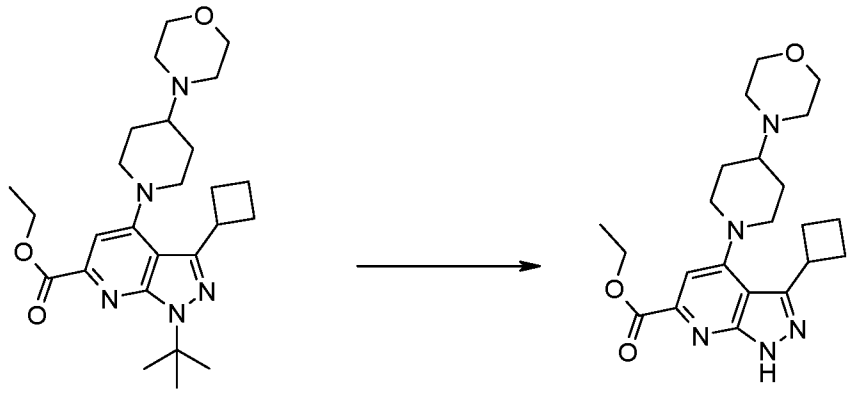
[00535] *Step 1: E390: ethyl 3-cyclobutyl-1-[2-(3,6-dihydro-2H-pyran-4-yl)pyridin-4-yl]-4-[4-(methoxymethyl)piperidin-1-yl]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate*

[00536] In a sealed tube, a suspension of E389 (110 mg, 0.23 mmol), 3,6-dihydro-2*H*-pyran-4-boronic pinacol ester (72 mg, 0.34 mmol), K_3PO_4 (146 mg, 0.69 mmol) and Pd(Amphos)Cl_2 ([887919-35-9], 16 mg, 23 µmol) in dioxane (3 mL) and water (0.5 mL) was degassed with N_2 at room temperature for 2 minutes. The reaction mixture was heated at 100 °C for 3 hours. The mixture was cooled to RT and then concentrated under reduced pressure. The crude sample was purified by flash column chromatography eluted with ethyl acetate/*n*-heptane to give the titled compound E390.

[00537] *Step 2: E391: ethyl 3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-[2-(oxan-4-yl)pyridin-4-yl]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate*

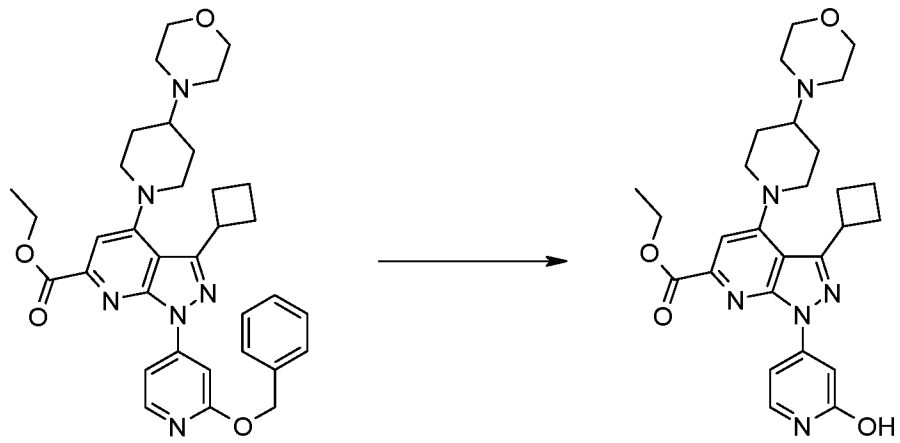
[00538] A suspension of E390 (60 mg, 0.11 mmol) and palladium hydroxide on carbon (20 mg) in ethanol was hydrogenated for 6 hours. The reaction mixture was filtered over Celpure® and washed with ethyl acetate. The filtrate was concentrated in vacuo, and the residue was purified by silica gel chromatography eluted with ethyl acetate/*n*-heptane to give the titled compound E391.

Synthesis of E393: ethyl 3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate



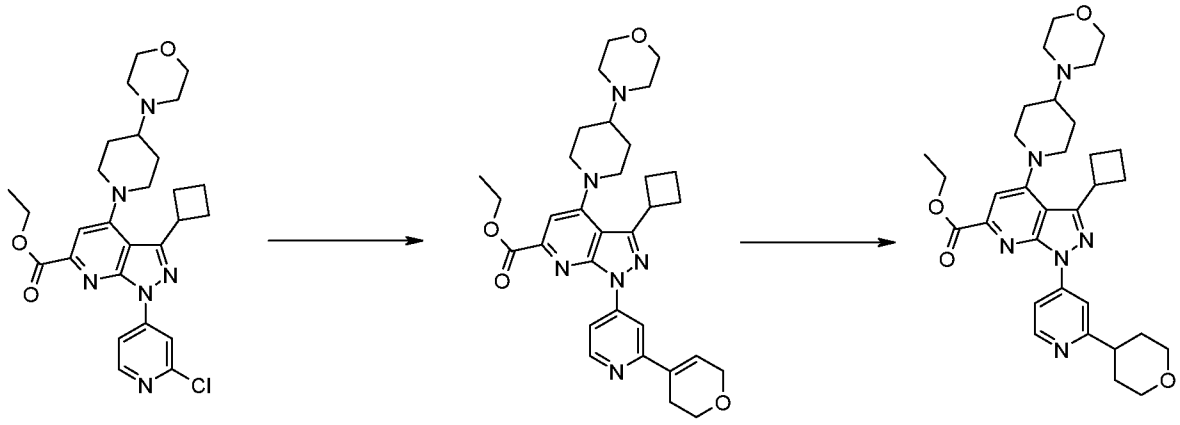
[00539] Trifluoromethanesulfonic acid (860 µL, 10 mmol) was added dropwise at RT to a solution of E392 (1 g, 2 mmol) in dichloromethane (10 mL). The reaction mixture was stirred for 4 hours and poured into a mixture of saturated aqueous $NaHCO_3$ and water (1:1, 10 mL). The aqueous phase was extracted twice with dichloromethane/isopropanol (95/5, 20 mL). The combined organic phases were combined, dried over sodium sulfate, filtered and concentrated under reduced pressure to give the titled compound as a colorless solid.

Synthesis of E402: ethyl 3-cyclobutyl-1-(2-hydroxypyridin-4-yl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate



[00540] A suspension of E401 (75 mg, 0.12 mmol) and palladium hydroxide on carbon (10 mg) in THF was hydrogenated for 20 hours. The reaction mixture was filtered over Celpure® that was washed with dichloromethane/methanol. The filtrate was concentrated in vacuo to give the titled compound E402.

Synthesis of E407: ethyl 3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-[2-(oxan-4-yl)pyridin-4-yl]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate



[00541] *Step 1: ethyl 3-cyclobutyl-1-[2-(3,6-dihydro-2H-pyran-4-yl)pyridin-4-yl]-4-[4-(morpholin-4-yl)piperidin-1-yl]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate*

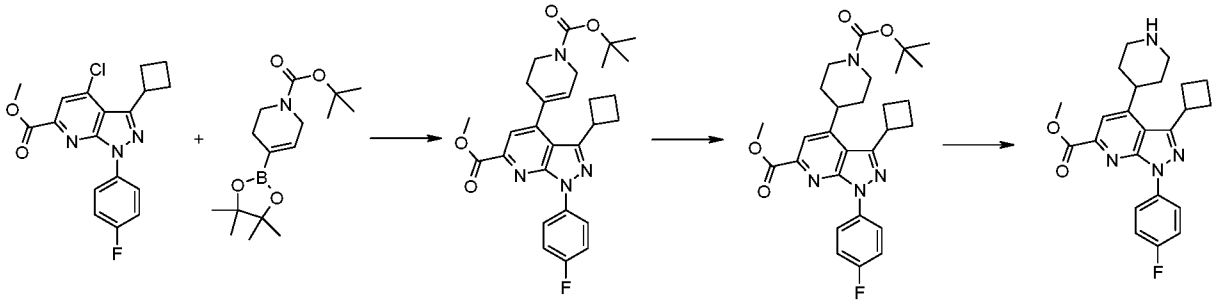
[00542] In a sealed tube, a suspension of E406 (110 mg, 0.21 mmol), 3,6-dihydro-2*H*-pyran-4-boronic pinacol ester (72 mg, 0.34 mmol), K_3PO_4 (146 mg, 0.69 mmol) and Pd(Amphos)Cl_2 ([887919-35-9], 16 mg, 23 µmol) in dioxane (3 mL) and water (0.5 mL) was degassed with N_2 at room temperature for 2 minutes. The reaction mixture was heated at 100 °C for 20 hours. The mixture was cooled to RT, and the mixture was concentrated under reduced pressure. The crude

sample was purified by flash column chromatography eluted with ethyl acetate/*n*-heptane to give the titled compound.

[00543] *Step 2: ethyl 3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-[2-(oxan-4-yl)pyridin-4-yl]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate*

[00544] A suspension of ethyl 3-cyclobutyl-1-[2-(3,6-dihydro-2*H*-pyran-4-yl)pyridin-4-yl]-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate (54 mg, 0.94 mmol) and palladium hydroxide on carbon (15 mg) in ethanol/THF (1 : 1, 10 mL) was hydrogenated for 6 hours. The reaction mixture was filtered over Celpure® that was washed with ethyl acetate, and the filtrate was concentrated in vacuo. The residue was purified by silica gel chromatography eluted with ethyl acetate/*n*-heptane to give the titled compound, E407.

Synthesis of E413: methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-(piperidin-4-yl)-1H-pyrazolo[3,4-b]pyridine-6-carboxylate



[00545] *Step 1: methyl 4-[1-(tert-butoxycarbonyl)-1,2,3,6-tetrahydropyridin-4-yl]-3-cyclobutyl-1-(4-fluorophenyl)-1H-pyrazolo[3,4-b]pyridine-6-carboxylate*

[00546] A suspension of methyl 4-chloro-3-cyclobutyl-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate (HP19, 2.0 g, 5.75 mmol, 1.0 equiv), *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,6-dihydro-2*H*-pyridine-1-carboxylate (CAS 286961-14-6, 3.6 g, 11.5 mmol, 2.0 equiv), K_2CO_3 (2.4 g, 17.25 mmol, 3.0 equiv) and $Pd(dppf)Cl_2$ (CAS : 72287-26-4, 939 mg, 1.15 mmol, 0.2 equiv) in anhydrous DMF (15 mL) was degassed with nitrogen at room temperature for 2 minutes. The reaction mixture was refluxed for 20 hours. The mixture was cooled to RT, poured into 150 mL of iced water and diluted with ethyl acetate. The two phases were separated, and the aqueous phase was extracted again with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, filtered and concentrated. The

crude residue was purified by silica gel chromatography (heptane/ethyl acetate: 100/0 to 80/20) to give the titled compound.

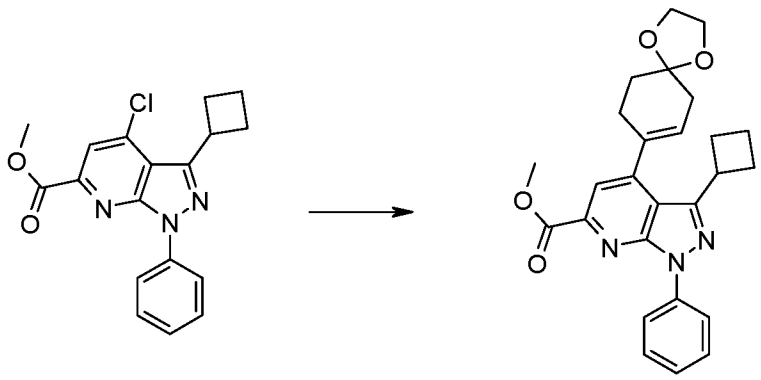
[00547] *Step 2: methyl 4-[1-(tert-butoxycarbonyl)piperidin-4-yl]-3-cyclobutyl-1-(4-fluorophenyl)-1H-pyrazolo[3,4-b]pyridine-6-carboxylate*

[00548] A suspension of compound from Step 1 (2.44 g, 4.93 mmol, 1.0 equiv) and platinum (IV) oxide (CAS 1314-15-4, 1.2 g) in acetic acid (240 mL) was stirred at RT under a hydrogen atmosphere (balloon) for 20 hours. The reaction mixture was filtered over Celpure® P65. Solids were washed with ethyl acetate, and the filtrate was concentrated in vacuo. The crude residue was purified by silica gel chromatography (heptane/ethyl acetate: 100/0 to 80/20) to give the title compound.

[00549] *Step 3: methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-(piperidin-4-yl)-1H-pyrazolo[3,4-b]pyridine-6-carboxylate*

[00550] Methyl 4-[1-(*tert*-butoxycarbonyl)piperidin-4-yl]-3-cyclobutyl-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate (2.75 g, 5.4 mmol, 1 equiv) was dissolved in 4 M HCl in dioxane (40 mL, 162.2 mmol, 30 equiv), and the solution was stirred at RT for 2 hours. The solvent was concentrated under reduced pressure. The residue was dissolved in a minimum of methanol and poured into diethyl ether (500 mL). The precipitate was filtered, washed with diethyl ether and dried at 40 °C under reduced pressure to give the titled compound, E413.

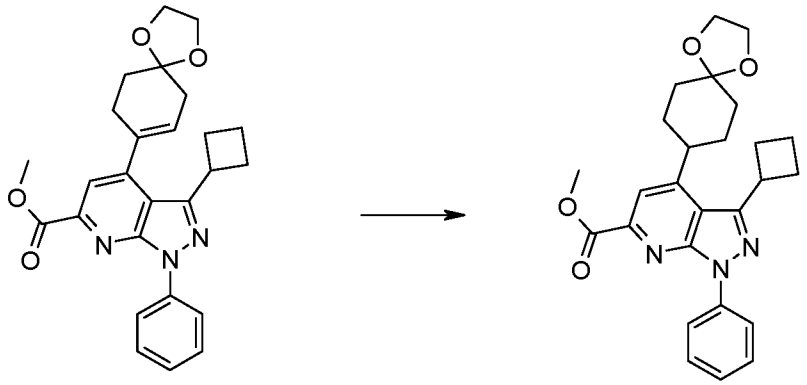
Synthesis of E430: methyl 3-cyclobutyl-4-(1,4-dioxaspiro[4.5]dec-7-en-8-yl)-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxylate



[00551] In a sealed tube, a suspension of HP02 (1 g, 2.92 mmol), 1,4-dioxa-spiro[4,5]dec-7-en-8-boronic acid, pinacol ester ([680596-79-6], 1.01 g, 3.8 mmol), K_3PO_4 (1.86 g, 8.77 mmol),

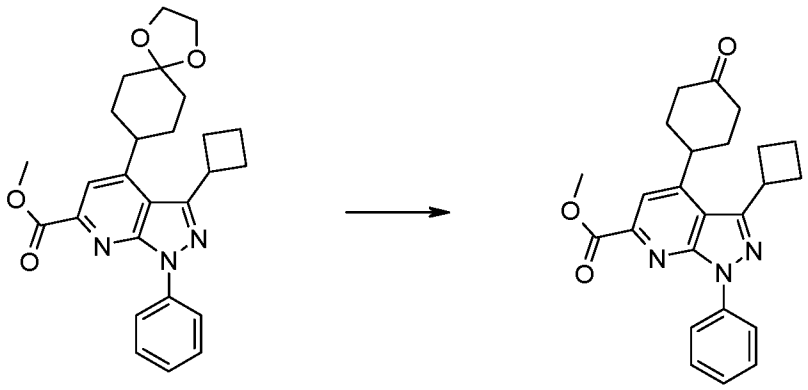
$Pd(OAc)_2$ ([3375-31-3], 330 mg, 0.14 mmol), and SPhos ([657408-07-6], 150 mg, 0.365 mmol) in toluene (22 mL) and water (6 mL) was degassed with N_2 at room temperature for 5 minutes. The reaction mixture was stirred at RT for 2 hours. Additional $Pd(OAc)_2$ ([3375-31-3], 330 mg, 0.14 mmol) and SPhos ([657408-07-6], 150 mg, 0.365 mmol) were added. The stirring at RT was continued for 20 hours. Pd(OAc)2 ([3375-31-3], 165 mg, 0.07 mmol) and SPhos ([657408-07-6], 75 mg, 0.18 mmol) were again added, and the reaction mixture was heated at 100 °C for 1 hour. The reaction mixture was cooled to RT, diluted with ethyl acetate and filtered. The filtrate was washed successively with water and a saturated aqueous solution of NaCl. The organic phase was separated, dried over sodium sulfate, filtered and concentrated under reduced pressure. The crude residue was purified by flash column chromatography on silica gel eluting with ethyl acetate/*n*-heptane to give the titled compound.

Synthesis of E431: methyl 3-cyclobutyl-4-(1,4-dioxaspiro[4.5]decan-8-yl)-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxylate



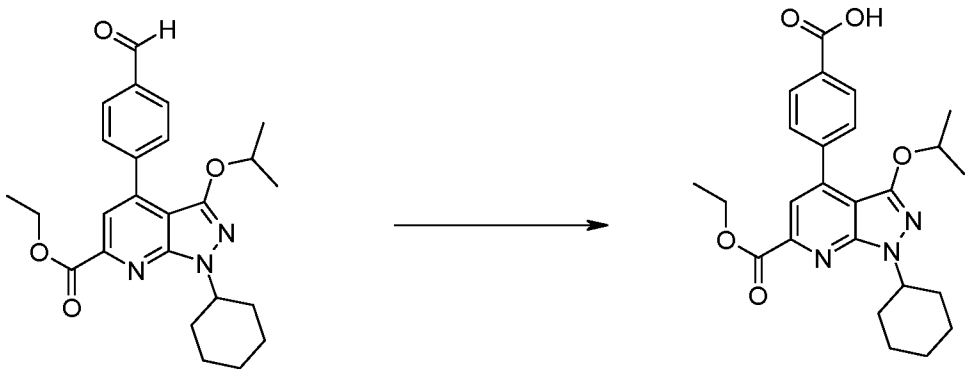
[00552] A suspension of E430 (823 mg, 1.85 mmol) and palladium hydroxide on carbon ([12135-22-7], 280 mg) in THF/MeOH (25 mL, 2/1) was hydrogenated for 20 hours. The reaction mixture was filtered over Celpure® which was washed with DCM. The filtrate was concentrated in vacuo. The residue was purified by silica gel chromatography eluting with ethyl acetate/*n*-heptane to give the titled compound E431.

Synthesis of E432: methyl 3-cyclobutyl-1-[(3E,5Z)-hepta-1,3,5-trien-4-yl]-4-(4-oxocyclohexyl)-1H-pyrazolo[3,4-b]pyridine-6-carboxylate



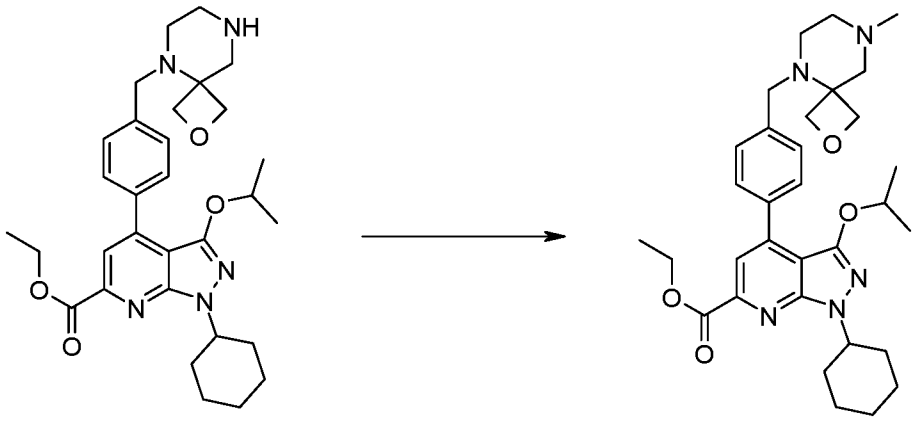
[00553] The ester, E431 (732 mg, 1.64 mmol), was dissolved in DCM and TFA (2.2 mL, 3 volumes) was added dropwise at RT. The solution was stirred for 48 hours and then diluted with DCM. The mixture was washed with a saturated aqueous solution of $NaHCO_3$. The organic phase was separated, dried over sodium sulfate, filtered and concentrated in vacuo. The residue was purified by silica gel chromatography eluting with ethyl acetate/*n*-heptane to give the titled compound E432.

Synthesis of E438: 4-{1-cyclohexyl-6-(ethoxycarbonyl)-3-[(propan-2-yl)oxy]-1H-pyrazolo[3,4-b]pyridin-4-yl}benzoic acid



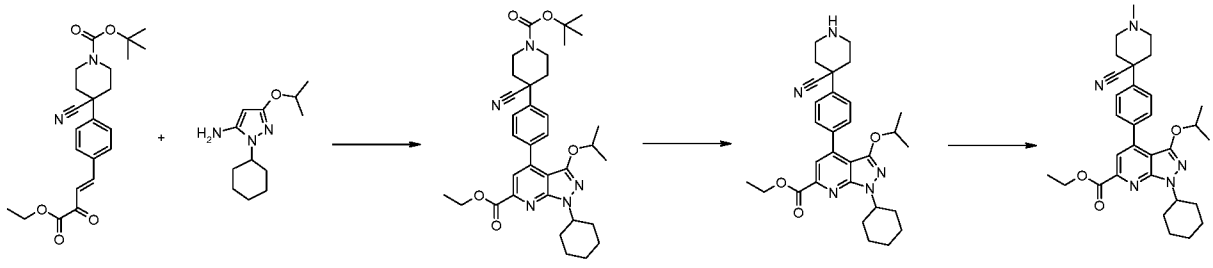
[00554] A mixture of aldehyde E425 (27 mg, 62 µmol), sulfamic acid ([226-18-8], 17 mg, 168 µmol), and sodium chlorite ([7758-19-2], 17 mg, 188 µmol) in THF/water (3.3 mL, 10/1) was stirred at RT for 1 hour. The reaction mixture was diluted with DCM (20 mL) and washed with water (20 mL). The organic phase was dried over sodium sulfate, filtered and evaporated under reduced pressure. The titled compound was used as such in the next step.

Synthesis of E444: ethyl 1-cyclohexyl-4-{4-[(8-methyl-2-oxa-5,8-diazaspiro[3.5]nonan-5-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate



[00555] Iodomethane (3 µL, 48 µmol) was added at RT to a stirred suspension of E443 (22 mg, 40 µmol) and cesium carbonate (33 mg, 100 µmol) in DMF (2 mL). The reaction mixture was stirred for 20 hours. The reaction mixture was partitioned between water and ethyl acetate. The organic phase was dried over sodium sulfate, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography eluting with ethyl acetate/DCM/MeOH (100/0/0 to 0/90/10) to give the titled compound.

Synthesis of E445: ethyl 4-[4-(4-cyano-1-methylpiperidin-4-yl)phenyl]-1-cyclohexyl-3-[(propan-2-yl)oxy]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate



[00556] *Step 1: ethyl 4-{4-[1-(tert-butoxycarbonyl)-4-cyanopiperidin-4-yl]phenyl}-1-cyclohexyl-3-[(propan-2-yl)oxy]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate*

[00557] A solution of ALP38 (305 mg, 0.74 mmol) and AMP95 (575 mg, 0.77 mmol) in *N*-methylpyrrolidine (4 mL) was heated at 110 °C for 24 hours in an opened vessel. The reaction mixture was cooled to RT, and the mixture was concentrated in vacuo. The residue was partitioned between ethyl acetate and water. The organic phase was separated, dried over

sodium sulfate, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel eluting with ethyl acetate/*n*-heptane to give the titled compound.

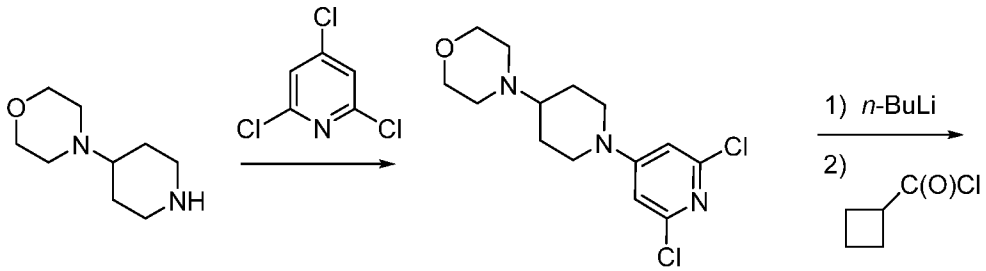
[00558] *Step 2: ethyl 4-[4-(4-cyanopiperidin-4-yl)phenyl]-1-cyclohexyl-3-[(propan-2-yl)oxy]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate.*

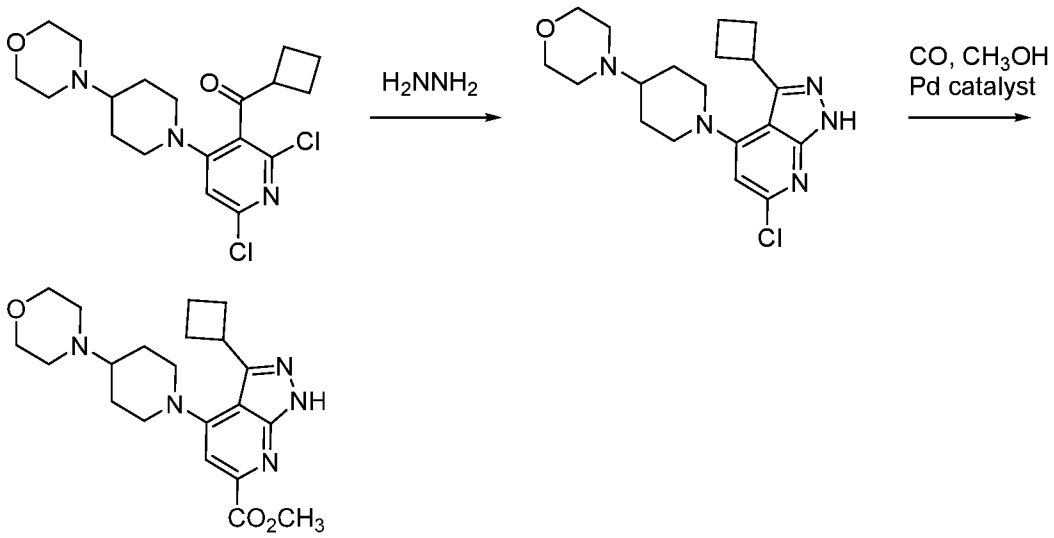
[00559] Trifluoroacetic acid (1 mL) was added to a solution of the *tert*-butoxycarbonyl protected compound from Step 1 (230 mg, 0.37 mmol) in DCM (10 mL). The solution was stirred at RT for 2 hours. The reaction mixture was diluted with toluene (5mL) and then concentrated under reduced pressure. The residue was partitioned between ethyl acetate, water, and a phosphate buffer solution (pH 6.2). The organic phase was dried over sodium sulfate, filtered and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel eluting with ethyl acetate/*n*-heptane to give the titled compound.

[00560] *Step 3: ethyl 4-[4-(4-cyano-1-methylpiperidin-4-yl)phenyl]-1-cyclohexyl-3-[(propan-2-yl)oxy]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate*

[00561] Iodomethane (2 µL, 32 µmol) was added at RT to a stirred suspension of the compound from Step 2 (15 mg, 29 µmol) and cesium carbonate (33 mg, 100 µmol) in DMF (2 mL). The reaction mixture was stirred for 2 hours. The reaction mixture was partitioned between water and DCM. The organic phase was dried over sodium sulfate, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography eluting with ethyl acetate/DCM/MeOH (100/0/0 to 0/90/10) to give the titled compound.

Synthesis of E509: methyl 3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate





[00562] *Step 1: 4-[1-(2,6-dichloropyridin-4-yl)piperidin-4-yl]morpholine*

[00563] *N*-Ethyl-*N*-isopropylpropan-2-amine (22.91 mL, 132 mmol) was added to a suspension of 2,4,6-trichloropyridine (12 g, 65.8 mmol) and 4-(piperidin-4-yl)morpholine (13.44 g, 79 mmol) in acetonitrile (120 mL). The reaction mixture was heated to 60 °C and stirred for 16 hours. Upon cooling to room temperature, the precipitate was collected by filtration. The crude solid was then precipitated from EtOAc to give the titled compound. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 6.59 (s, 2H), 3.89 – 3.79 (m, 2H), 3.77 – 3.69 (m, 4H), 2.96 (ddd, J = 13.3, 11.8, 2.8 Hz, 2H), 2.60 – 2.52 (m, 4H), 2.45 (tt, J = 10.8, 3.7 Hz, 1H), 1.95 (ddd, J = 12.9, 3.9, 1.9 Hz, 2H), 1.61 – 1.48 (m, 2H); MS (APCI+) *m/z* 316.2 $(M+H)^+$.

[00564] *Step 2: cyclobutyl{2,6-dichloro-4-[4-(morpholin-4-yl)piperidin-1-yl]pyridin-3-yl}methanone*

[00565] *n*-Butyllithium (19.2 mL, 26.9 mmol) was added in 5 mL portions to a stirred solution of 4-[1-(2,6-dichloropyridin-4-yl)piperidin-4-yl]morpholine (7.95 g, 25.1 mmol) in THF (160 mL) at –78 °C. After stirring at this temperature for 1.5 hours, cyclobutanecarbonyl chloride (1.42 g, 11.9 mmol) was added rapidly, and the reaction mixture was stirred for 10 minutes. To obtain higher conversion, sequential additions of *n*-butyllithium and cyclobutanecarbonyl chloride were performed in the same manner. Addition 1: *n*-butyllithium (13.0 mL, 18.2 mmol) and cyclobutanecarbonyl chloride (0.97 g, 8.1 mmol); Addition 2: *n*-butyllithium (9.2 mL, 12.9 mmol) and cyclobutanecarbonyl chloride (0.68 g, 5.6 mmol); Addition 3: *n*-butyllithium (6.9 mL, 9.7 mmol) and cyclobutanecarbonyl chloride (0.51 g, 4.2 mmol); Addition 4: *n*-butyllithium (5.7 mL, 8.0 mmol) and cyclobutanecarbonyl chloride (0.41 g, 3.4 mmol). Upon completion of

the last addition, the excess *n*-butyl lithium was quenched with water (200 mL), and the mixture was extracted with ethyl acetate (3 x 100 mL). The combined organic fractions were washed with brine (100 mL), dried over sodium sulfate, and concentrated in vacuo. The residue was purified by column chromatography (0-5% 95/5 MeOH/30% aqueous NH_3 in DCM) to give the titled compound. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 6.76 (s, 1H), 3.80 – 3.65 (m, 5H), 3.50 – 3.40 (m, 2H), 2.98 – 2.76 (m, 2H), 2.62 – 2.50 (m, 4H), 2.50 – 2.37 (m, 2H), 2.29 (tt, J = 11.0, 3.8 Hz, 1H), 2.22 – 2.08 (m, 2H), 2.08 – 1.93 (m, 2H), 1.93 – 1.83 (m, 2H), 1.52 (dddd, J = 14.8, 12.8, 7.5, 3.8 Hz, 2H); MS (APCI+) *m/z* 398.2 $(M+H)^+$.

[00566] *Step 3: 6-chloro-3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1H-pyrazolo[3,4-b]pyridine*

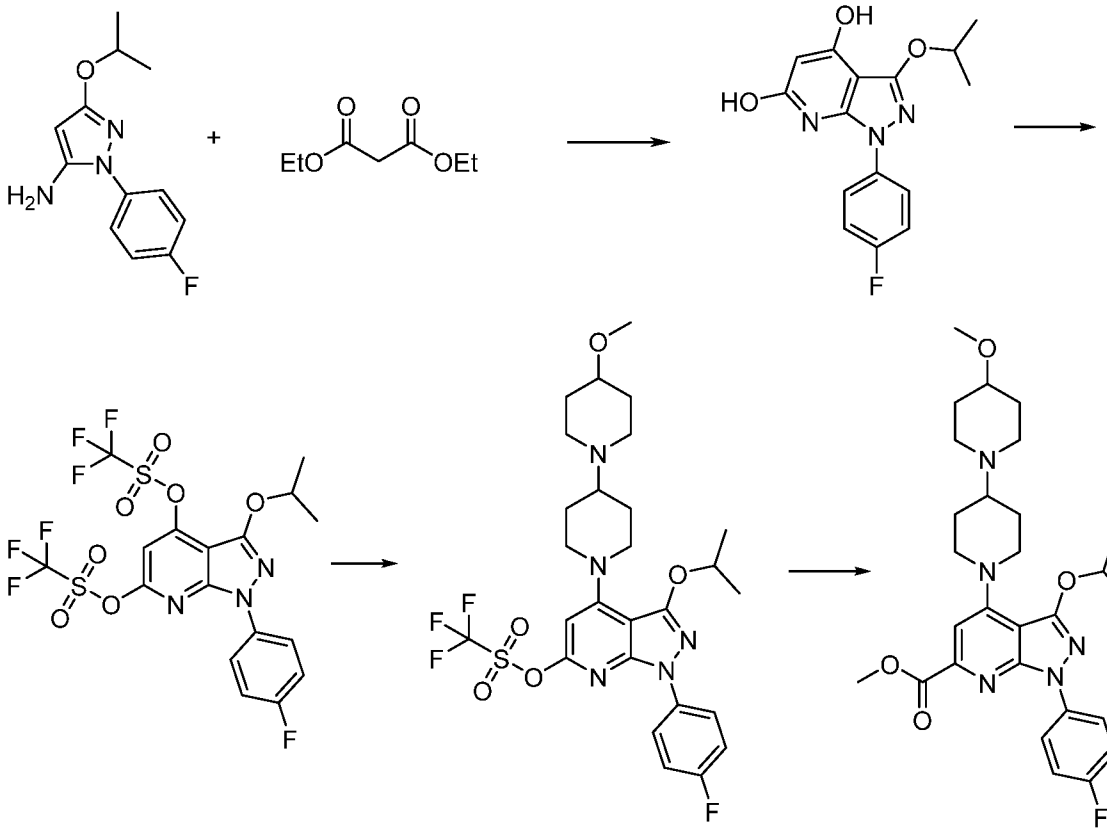
[00567] Hydrazine (35% in water, 3.10 mL, 33.9 mmol) was added to cyclobutyl{2,6-dichloro-4-[4-(morpholin-4-yl)piperidin-1-yl]pyridin-3-yl}methanone (4.5 g, 11.30 mmol) in EtOH (32 mL). The reaction mixture was heated to reflux for 14 hours. Upon cooling to –5 °C, the precipitate was isolated by filtration. The filter cake was rinsed with cold EtOH to give the titled compound. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 10.21 (br s, 1H), 6.45 (s, 1H), 3.94 – 3.76 (m, 5H), 3.63 (d, J = 12.4 Hz, 2H), 2.84 (td, J = 12.4, 2.3 Hz, 2H), 2.71 – 2.59 (m, 4H), 2.58 – 2.44 (m, 2H), 2.44 – 2.31 (m, 3H), 2.14 – 1.97 (m, 4H), 1.85 – 1.70 (m, 2H); MS (APCI+) *m/z* 376.2 $(M+H)^+$.

[00568] *Step 4: methyl 3-cyclobutyl-4-(4-morpholinopiperidin-1-yl)-1H-pyrazolo[3,4-b]pyridine-6-carboxylate*

[00569] Into a 600 mL Parr reactor was charged 6-chloro-3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine (3.4 g, 9.05 mmol), followed by THF (170 mL) and MeOH (170 mL). 1,1'-Bis(diphenylphosphino)ferrocene-palladium (II) dichloride dichloromethane complex (0.739 g, 0.905 mmol), and triethylamine (2.52 mL, 18.09 mmol) were added to give a suspension. The reaction vessel was purged with argon followed by CO, pressurized to 100 psig with CO, and heated to 80 °C. After 8 hours, the reaction mixture was cooled to room temperature, diluted with CH_2Cl_2 (800 mL), and filtered. The filtrate was concentrated in vacuo, and the residue was dissolved in CH_2Cl_2 (800 mL). The organic mixture was washed with saturated aqueous $NaHCO_3$ (300 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was slurried in EtOAc to give the titled compound. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 10.98 (br s, 1H), 7.37 (s, 1H), 4.08 (s, 3H), 3.96 (p, J = 8.4 Hz,

1H), 3.83 – 3.76 (m, 4H), 3.70 (d, J = 12.3 Hz, 2H), 2.92 (t, J = 11.8 Hz, 2H), 2.66 (t, J = 4.7 Hz, 4H), 2.55 (dq, J = 11.3, 9.0 Hz, 2H), 2.44 – 2.31 (m, 3H), 2.15 – 2.00 (m, 4H), 1.88 – 1.74 (m, 2H); MS (APCI+) *m/z* 400.3 $(M+H)^+$.

[00570] *Synthesis of E511: methyl 1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-3-[(propan-2-yl)oxy]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate*



[00571] *Step 1: 1-(4-fluorophenyl)-3-[(propan-2-yl)oxy]-1H-pyrazolo[3,4-b]pyridine-4,6-diol*

[00572] In a sealed tube, a suspension of AMP96 (215 mg, 0.91 mmol) and diethyl malonate ([105-53-3], 418 µL, 2.75 mmol) in Dowtherm® A was heated at 200 °C 4 hours. The reaction mixture was cooled down to 70-80 °C and poured onto a stirring solution of *n*-heptane (200 mL). The precipitate was collected by filtration, washed with *n*-heptane and dried at 40 °C under reduced pressure to give the titled compound.

[00573] *Step 2: 1-(4-fluorophenyl)-3-[(propan-2-yl)oxy]-1H-pyrazolo[3,4-b]pyridine-4,6-diyl bis(trifluoromethanesulfonate)*

[00574] Trifluoromethanesulfonic anhydride ([358-23-6], 302 µL, 1.8 mmol) was added dropwise to a solution of 1-(4-fluorophenyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-4,6-diol (270 mg, 0.9 mmol, Step 1) and pyridine (220 µL, 2.25 mmol) in acetonitrile (5 mL), maintaining the temperature around 20-25 °C. The reaction mixture was stirred at RT for 20 hours. The reaction mixture was diluted with DCM and extracted twice with a saturated aqueous solution of $NaHCO_3$. The organic phase was separated, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The resulting residue was purified by silica gel chromatography (*n*-heptane/ethyl acetate, 1/0 to 0/1) to yield the titled compound.

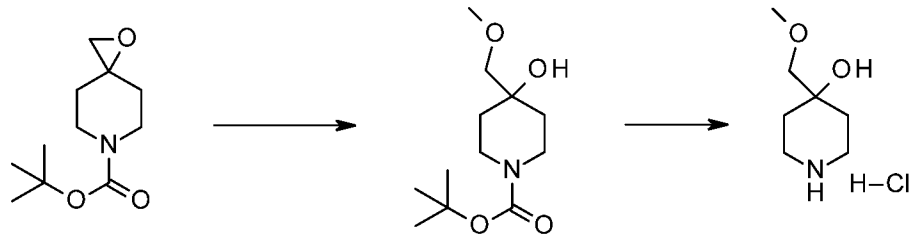
[00575] *Step 3: 1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-3-[(propan-2-yl)oxy]-1H-pyrazolo[3,4-b]pyridin-6-yl trifluoromethanesulfonate*

[00576] A mixture of 1-(4-fluorophenyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-4,6-diyl bis(trifluoromethanesulfonate) (29 mg, 50 µmol, Step 2), 4-methoxy-1-piperidin-4-ylpiperidine hydrochloride ([930603-98-8], 14 mg, 50 µmol) and DIPEA (35 µL, 200 µmol) in anhydrous DMSO (1 mL) was heated at 100 °C for 2 hours. The reaction mixture was cooled to RT and partitioned between ethyl acetate (50 mL) and water (30 mL). The organic phase was separated, dried over $MgSO_4$, filtered and concentrated in vacuo. The crude mixture was purified by flash chromatography on silica gel eluting with *n*-heptane/ethyl acetate (1/0 to 0/1) and ethyl acetate/(DCM/MeOH, 9/1) (1/0 to 0/1) to afford the titled compound.

[00577] *Step 4: methyl 1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-3-[(propan-2-yl)oxy]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate*

[00578] A pressured vessel was charged with 1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridin-6-yl trifluoromethanesulfonate (145 mg, 240 µmol, Step 3), Pd(dppf)Cl_2•DCM ([95464-05-4], 4 mg, 4.8 µmol), and triethylamine (66 µL, 500 µmol) in MeOH (5 mL). The system was loaded with CO (6 bars) and heated at 100 °C for 1 hour. The vessel was cooled down to RT, and the mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography eluting with a mixture of ethyl acetate/(DCM/MeOH, 9/1) (1/0 to 0/1) to give the titled compound.

Synthesis of AMI01: 4-(methoxymethyl)piperidin-4-ol hydrochloride



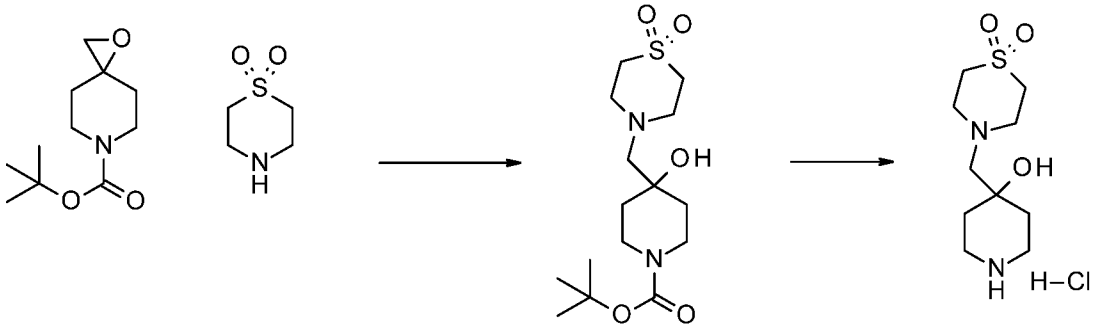
[00579] *Step 1: 4-Hydroxy-4-methoxymethyl-piperidine-1-carboxylic acid tert-butyl ester*

[00580] A suspension of *tert*-butyl 1-oxa-6-azaspiro[2.5]octane-6-carboxylate (CAS: 147804-30-6, 200 mg, 0.94 mmol) and sodium methoxide (61 mg, 1.13 mmol) in methanol (2 mL) was placed in a sealed tube and was heated at 100 °C for 20 hours. The reaction mixture was cooled to RT, acidified with acetic acid to pH 5-6, diluted with DCM and washed with water. The organic phase was separated using a phase separator and concentrated in vacuo. The titled compound was used as such in the next step without any further purification.

[00581] *Step 2: 4-Methoxymethyl-piperidin-4-ol hydrochloride*

4-Hydroxy-4-methoxymethyl-piperidine-1-carboxylic acid *tert*-butyl ester (206 mg, 0.84 mmol) was dissolved in dioxane (2 mL). 4 M HCl in dioxane (1.05 mL, 4.2 mmol) was added, and the solution was stirred at RT for 20 hours. The volatiles were removed under reduced pressure. The titled compound was used as such in the next step without any further purification.

Synthesis of AMI02: 4-[(1,1-dioxo-1,4-thiazinan-4-yl)methyl]piperidin-4-ol hydrochloride



[00582] *Step 1: tert-butyl 4-[(1,1-dioxo-1,4-thiazinan-4-yl)methyl]-4-hydroxy-piperidine-1-carboxylate*

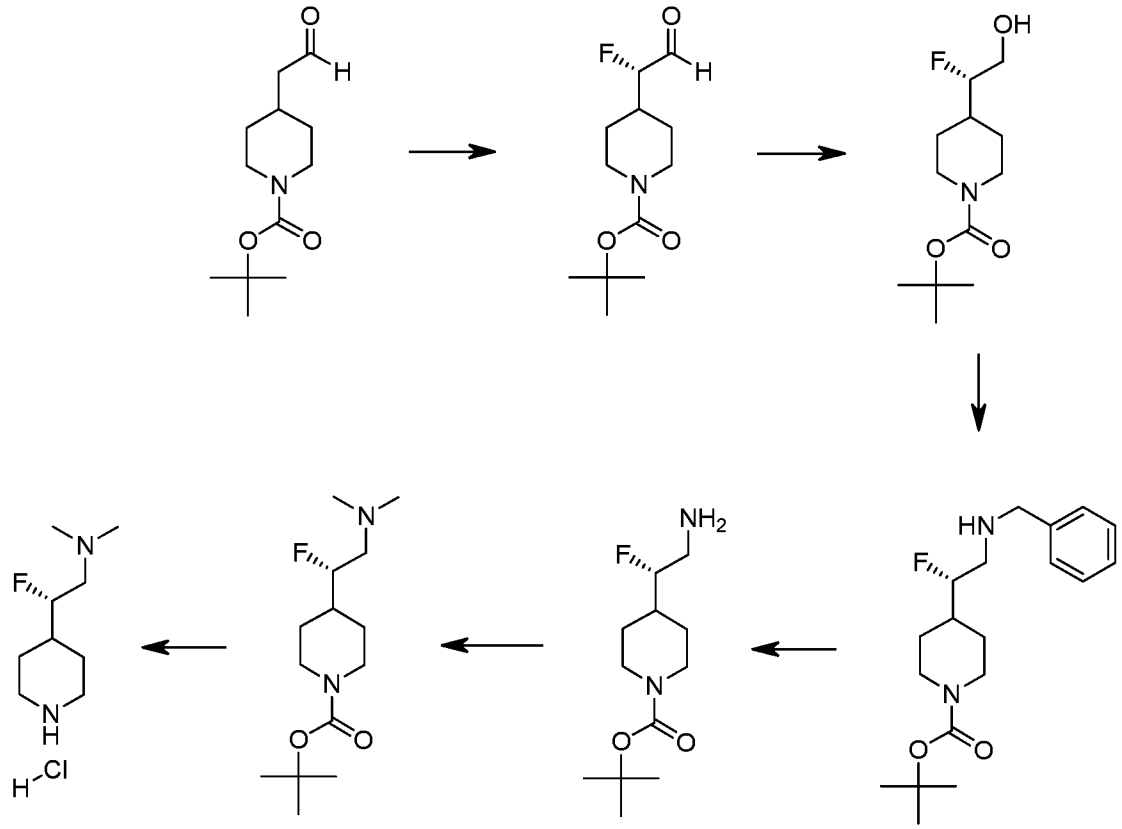
[00583] A solution of *tert*-butyl 1-oxa-6-azaspiro[2.5]octane-6-carboxylate (CAS: 147804-30-6, 150 mg, 0.7 mmol) and thiomorpholine 1,1-dioxide (CAS: 39093-93-1, 380 mg, 2.8 mmol) in

ethanol (2 mL) was placed in a sealed tube and was heated at 75 °C for 20 hours. The reaction mixture was cooled to RT, diluted with DCM and washed with water. The organic phase was separated using a phase separator and concentrated in vacuo. The titled compound was obtained by flash column chromatography eluting with DCM/MeOH.

[00584] *Step 2: 4-[(1,1-dioxo-1,4-thiazinan-4-yl)methyl]piperidin-4-ol hydrochloride*

[00585] *tert*-Butyl 4-[(1,1-dioxo-1,4-thiazinan-4-yl)methyl]-4-hydroxy-piperidine-1-carboxylate (215 mg, 0.62 mmol) was dissolved in dioxane (2 mL). 4 M HCl in dioxane (0.89 mL, 3.6 mmol) was added, and the solution was stirred at RT for 20 hours. The volatiles were removed under reduced pressure. The titled compound was used as such in the next step without any further purification.

Synthesis of AMI03: (2S)-2-fluoro-N,N-dimethyl-2-(4-piperidyl)ethanamine hydrochloride



[00586] *Step 1: (S)-tert-butyl 4-(1-fluoro-2-oxoethyl)piperidine-1-carboxylate*

[00587] To a suspension of *N*-fluoro-*N*-(phenylsulfonyl)benzenesulfonamide ((CAS 133745-75-2, 347 g, 1100 mmol) and (5*R*)-(+)-2,2,3-trimethyl-5-benzyl-4-imidazolidinone

dichloroacetic acid (CAS 857303-87-8, 76 g, 220 mmol) in THF and isopropyl alcohol at -20 °C was added a solution of *tert*-butyl 4-(2-oxoethyl)piperidine-1-carboxylate (250 g, 1100 mmol, CAS: 142374-19-4) in THF. The mixture was stirred at 10 °C for 16 h, diluted with hexane at -78 °C and filtered through silica, washed with hexane, then with saturated aqueous $NaHCO_3$, dried, filtered, and concentrated to give (*S*)-*tert*-butyl 4-(1-fluoro-2-oxoethyl)piperidine-1-carboxylate.

[00588] *Step 2: (S)-tert-butyl 4-(1-fluoro-2-hydroxyethyl)piperidine-1-carboxylate*

[00589] A solution of (*S*)-*tert*-butyl 4-(1-fluoro-2-oxoethyl)piperidine-1-carboxylate (10 g, 40.8 mmol) in dichloromethane (280 mL) and ethanol (220 mL) was stirred at 10 °C. Then, sodium borohydride (CAS 16940-66-2, 4.0 g, 105.7 mmol, 2.6 equiv) was added. The mixture was stirred at 10 °C for 1 hour, was diluted with water and extracted with dichloromethane. The organic layer was dried, filtered and concentrated, and the residue was purified by chromatography on silica gel (petroleum ether:ethyl acetate) to give (*S*)-*tert*-butyl 4-(1-fluoro-2-hydroxyethyl)piperidine-1-carboxylate.

[00590] *Step 3: (S)-tert-butyl 4-(2-(benzylamino)-1-fluoroethyl)piperidine-1-carboxylate*

[00591] Trifluoromethanesulfonic anhydride (CAS 358-23-6, 5.70 g, 20.22 mmol, 1.0 equiv) was added to a solution of (*S*)-*tert*-butyl 4-(1-fluoro-2-hydroxyethyl)piperidine-1-carboxylate (5 g, 20.22 mmol) and 2,6-dimethylpyridine (CAS 108-48-5,2.166 g, 20.22 mmol, 1.0 equiv) in dichloromethane at 0 °C. The mixture was stirred at 0 °C for 0.5 h. A separated round bottom flask was charged with benzylamine (2.166 g, 20.22 mmol, 1.0 equiv) in dichloromethane at 0 °C. The solution of the triflate was then added slowly at 0 °C. The reaction mixture was stirred at 25 °C for 12 hours, quenched with a saturated aqueous solution of sodium hydrogencarbonate, and extracted with dichloromethane. The organic fraction was concentrated. The residue was purified on silica gel chromatography, eluting with acetone/dichloromethane to give (*S*)-*tert*-butyl 4-(2-(benzylamino)-1-fluoroethyl)piperidine-1-carboxylate.

[00592] *Step 4: (S)-tert-butyl 4-(2-amino-1-fluoroethyl)piperidine-1*-carboxylate

[00593] To a solution of (*S*)-*tert*-butyl 4-(2-(benzylamino)-1-fluoroethyl)piperidine-1-carboxylate (4.5 g, 13.38 mmol) in methanol was added Pd/C, then the solution was stirred at 35 °C under hydrogen atmosphere (45 psi) for 12 hours. The mixture was filtered and concentrated to give (*S*)-*tert*-butyl 4-(2-amino-1-fluoroethyl)piperidine-1-carboxylate.

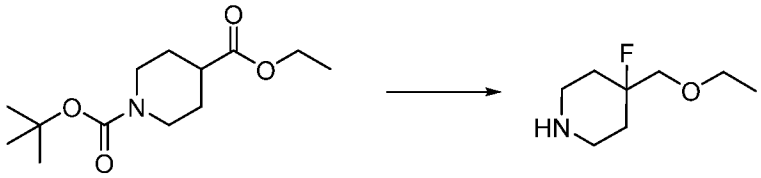
[00594] *Step 5: (S)-tert-butyl 4-(2-(dimethylamino)-1-fluoroethyl)piperidine-1-carboxylate*

[00595] To a mixture of (*S*)-*tert*-butyl 4-(2-amino-1-fluoroethyl)piperidine-1-carboxylate (3.0 g, 12.18 mmol) in methanol was added paraformaldehyde (CAS 30525-89-4, 1.828 g, 60.9 mmol, 5.0 equiv) followed by three drops of acetic acid. The reaction mixture stirred for 1 hour. Then sodium cyanoborohydride (CAS 25895-60-7, 1.148 g, 18.27 mmol, 1.5 equiv) was added, and the mixture was stirred for 12 hours. The reaction mixture was filtered and concentrated, and the residue was purified by column chromatography on silica gel (DCM/MeOH) to afford (*S*)-*tert*-butyl 4-(2-(dimethylamino)-1-fluoroethyl)piperidine-1-carboxylate

[00596] *Step 6: (S)-2-fluoro-N,N-dimethyl-2-(piperidin-4-yl)ethanamine hydrochloride*

[00597] To a solution of (*S*)-*tert*-butyl 4-(2-(dimethylamino)-1-fluoroethyl)piperidine-1-carboxylate (2 g, 7.29 mmol) in MeOH was added 4 N hydrogen chloride in methanol (10 mL, 40 mmol, 5.5 equiv), and the mixture was stirred at RT for 2 hours. Then the solution was concentrated to give (*S*)-2-fluoro-*N*,*N*-dimethyl-2-(piperidin-4-yl)ethanamine hydrochloride.

Synthesis of AMI04: 4-(ethoxymethyl)-4-fluoro-piperidine



[00598] *Step 1: 1-tert-butyl 4-ethyl 4-fluoropiperidine-1,4-dicarboxylate*

[00599] In a 100 mL round-bottomed flask was combined 1-*tert*-butyl 4-ethyl piperidine-1,4-dicarboxylate (1 g, 3.89 mmol) and THF (10 mL). The solution was cooled to -78 °C, and sodium hexamethyldisilazide (6 mL of 1 M THF solution, 6.00 mmol) was added slowly via syringe. After 60 min, *N*-fluoro-*N*-(phenylsulfonyl)benzenesulfonamide (2 g, 6.34 mmol) in THF (3 mL) was added. After 2 h, dichloromethane/water (1:1, 40 mL) was added. The aqueous layer was extracted with dichloromethane, and the combined organic fractions were dried over Na_2SO_4, filtered, and concentrated in vacuo.

[00600] *Step 2: tert-butyl 4-fluoro-4-(hydroxymethyl)piperidine-1-carboxylate*

[00601] A solution of 1-*tert*-butyl 4-ethyl 4-fluoropiperidine-1,4-dicarboxylate (1.5g, 5.45 mmol) in THF (5 mL) was cooled to 0 °C, and then 1 M $LiAlH_4$ in THF (3.81 mL, 3.81 mmol) was added dropwise. The reaction mixture was warmed up to RT and stirred for 2 h. Water (0.9 mL) was added to the reaction mixture dropwise followed by 2 N NaOH (0.3 mL). The

mixture was stirred for another 30 minutes, and then solid removed by filtration through diatomaceous earth and washed with EtOAc. The filtrate was washed with brine, dried over Na_2SO_4, and concentrated from acetonitrile under vacuum several time to remove the water to afford *tert*-butyl 4-fluoro-4-(hydroxymethyl)piperidine-1-carboxylate.

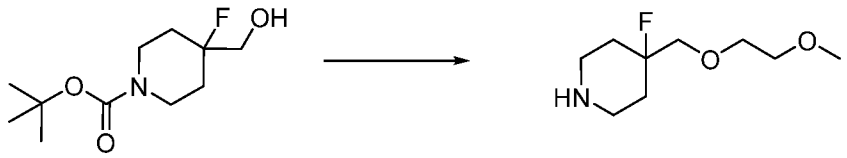
[00602] *Step 3: tert-butyl 4-(ethoxymethyl)-4-fluoropiperidine-1-carboxylate*

[00603] *tert*-Butyl 4-fluoro-4-(hydroxymethyl)piperidine-1-carboxylate (30 g, 129 mmol) was first treated with sodium hydride (6.17 g, 154 mmol) DMF (500 mL), and then iodoethane (24.07 g, 154 mmol) was added at room temperature. The reaction mixture was stirred at 25 °C for 12 h. The mixture was washed with H_2O and extracted with EtOAc, and then the combined organic phases were washed with H_2O, and brine. The organic fraction was dried Na_2SO_4, filtered and concentrated to give *tert*-butyl 4-(ethoxymethyl)-4-fluoropiperidine-1-carboxylate (26.9 g, 103 mmol, 80% purity).

[00604] *Step 4: 4-(ethoxymethyl)-4-fluoro-piperidine*

[00605] A mixture of *tert*-butyl 4-(ethoxymethyl)-4-fluoropiperidine-1-carboxylate 26.9g, 103 mmol) in ethyl acetate (200 mL) was made acidic by addition of HCl in ethyl acetate solution at 0 °C. Then the mixture was allowed to warm to 15 °C and stirred at 15 °C for 3h. The reaction mixture was concentrated under vacuum to yield 4-(ethoxymethyl)-4-fluoropiperidine as a hydrochloride salt (15.27 g, 95 mmol, 92% yield).

Synthesis of AMI05: 4-fluoro-4-(2-methoxyethoxymethyl)piperidine



[00606] *Step 1: tert-butyl 4-fluoro-4-((2-methoxyethoxy)methyl)piperidine-1-carboxylate*

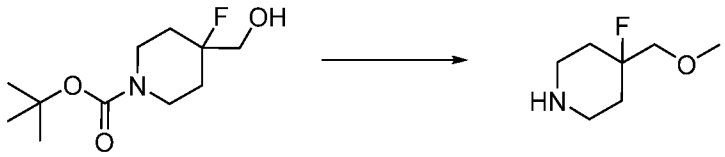
[00607] To a mixture of *tert*-butyl 4-fluoro-4-(hydroxymethyl)piperidine-1-carboxylate (30 g, 129 mmol, prepared as described in the synthesis of AMI04) in DMF (400 mL) was added sodium hydride (6.43 g, 161 mmol) at 0 °C. After 15 minutes, 1-bromo-2-methoxyethane (35.7 g, 257 mmol) was added at 0 °C, and the mixture was stirred at 25 °C for 12 h. The mixture was quenched with 200 mL of aqueous NH_4Cl at 5 °C. The organic layer was separated, washed with water and brine, dried over Na_2SO_4, and concentrated. After column chromatography on silica gel (petroleum ether/EtOAc = 10:1 to petroleum ether/EtOAc = 2:1), *tert*-butyl 4-fluoro-4-

((2-methoxyethoxy)methyl)piperidine-1-carboxylate (20.5 g, 70.4 mmol, 54.% yield) was obtained.

[00608] *Step 2: 4-fluoro-4-(2-methoxyethoxymethyl)piperidine*

[00609] A solution of *tert*-butyl 4-fluoro-4-((2-methoxyethoxy)methyl)piperidine-1-carboxylate (20 g, 68.6 mmol) in 200 mL EtOAc was made acidic with HCl in EtOAc at room temperature. After TLC on silica gel (petroleum ether/EtOAc = 1:1) showed that the reaction was complete, the mixture was concentrated to afford the titled compound as a hydrochloride salt (15 g, 65.9 mmol, 96% yield).

Synthesis of AMI07: 4-fluoro-4-(methoxymethyl)piperidine



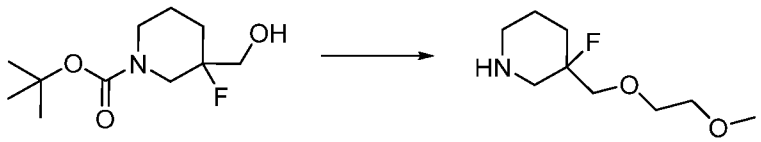
[00610] *Step 1: tert-butyl 4-fluoro-4-(methoxymethyl)piperidine-1-carboxylate*

[00611] To a mixture of *tert*-butyl 4-fluoro-4-(hydroxymethyl)piperidine-1-carboxylate (30 g, 129 mmol, prepared as described in the synthesis of AMI04) and NaH (3.09 g, 129 mmol) in THF (500 mL) was added iodomethane (41.9 g, 295 mmol) at room temperature, and then the mixture was stirred at 25 °C for 12 h, The reaction mixture was diluted with water and extracted with EtOAc. The combined organic phases were washed with water and brine. The organic fraction was dried over Na_2SO_4, filtered, and concentrated under vacuum. The residue was purified on a silica gel column eluted with petroleum ether/EtOAc=2:1 to give *tert*-butyl 4-fluoro-4-(methoxymethyl)piperidine-1-carboxylate (25 g, 101 mmol, 79% yield).

[00612] *Step 2: 4-fluoro-4-(methoxymethyl)piperidine*

[00613] A mixture of *tert*-butyl 4-fluoro-4-(methoxymethyl)piperidine-1-carboxylate (25 g, 101 mmol) in EtOAc (300 mL) was made acidic with HCl in EtOAc at 0 °C, and the mixture was allowed to warm to 15 °C and stirred at 15 °C for 3h. The reaction mixture was concentrated under vacuum to yield the titled compound as a hydrochloride salt (13 g, 70.8 mmol, 70.0% yield).

Synthesis of AMI08: 3-fluoro-3-(2-methoxyethoxymethyl)piperidine



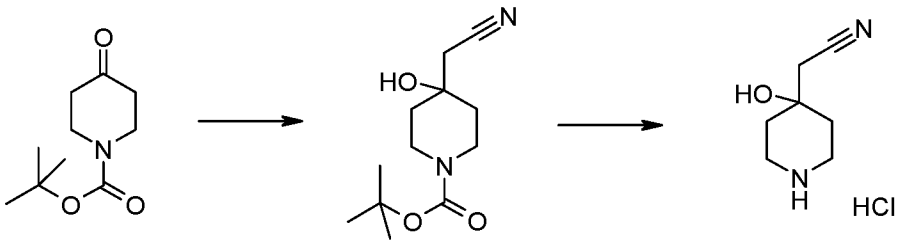
[00614] *Step 1: tert-butyl 3-fluoro-3-((2-methoxyethoxy)methyl)piperidine-1-carboxylate*

[00615] To a mixture of *tert*-butyl 3-fluoro-3-(hydroxymethyl)piperidine-1-carboxylate (25 g, 107 mmol) in THF (300 mL) was added NaH (2.57 g, 107 mmol) at 0 °C. After 15 minutes, 1-bromo-2-methoxyethane (29.8 g, 214 mmol) was added at 0 °C. The mixture was stirred at 25 °C for 12 h, and then the reaction was quenched by the addition of saturated aqueous NH_4Cl and extracted with EtOAc. The combined organic phases were washed with water and brine, dried over Na_2SO_4, filtered and concentrated in vacuum. The residue was added to a silica gel column eluted with hexanes:ethyl acetate (2:1) to give *tert*-butyl 3-fluoro-3-((2-methoxyethoxy)methyl)piperidine-1-carboxylate (22 g, 76 mmol, 70.5% yield).

[00616] *Step 2: 3-fluoro-3-(2-methoxyethoxymethyl)piperidine*

[00617] A mixture of *tert*-butyl 3-fluoro-3-((2-methoxyethoxy)methyl)piperidine-1-carboxylate (25 g, 86 mmol) in EtOAc (200 mL) was made acidic with HCl in EtOAc at 0 °C. The mixture was allowed to warm to 15 °C and stirred at 15 °C for 3h. The reaction mixture was concentrated under vacuum to the titled compound as a hydrochloride salt (15 g, 65.9 mmol, 77% yield).

Synthesis of AMI09: 2-(4-hydroxy-4-piperidyl)acetonitrile hydrochloride



[00618] *Step 1: tert-butyl 4-(cyanomethyl)-4-hydroxy-piperidine-1-carboxylate*

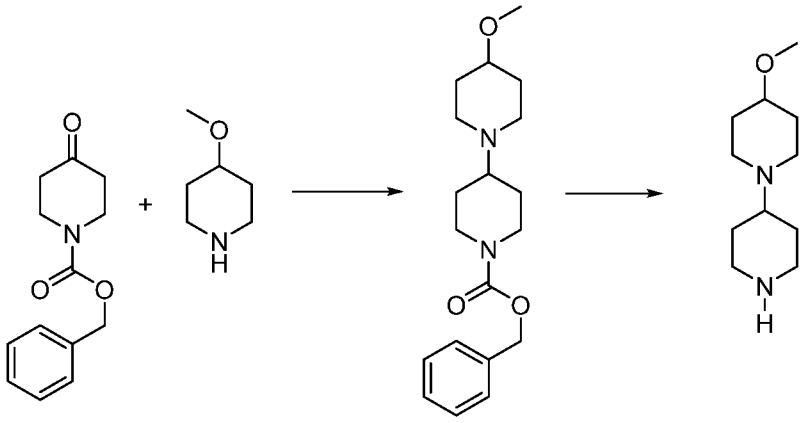
[00619] A flame-dried round bottom flask was cooled down to RT under argon. A solution of 1 M LiHMDS in THF (1.51 mL, 3.02 mmol, 2.0 equiv) was introduced into the flask and cooled down to -78 °C (acetone/dry ice bath). Dry MeCN (157 µL, 3.02 mmol, 2.0 equiv) in anhydrous THF (5 mL) was then added dropwise under argon, and the reaction mixture was stirred for 45 minutes at -78 °C. At this point, a solution of 1-(*tert*-butoxycarbonyl)-4-piperidone (300 mg,

1.51 mmol, 1.0 equiv) in dry THF (5 mL) was added dropwise, and the reaction mixture was stirred at -78 °C for 1 h. The reaction mixture was quenched with an aqueous saturated solution of ammonium chloride and diluted with ethyl acetate. The two phases were separated, and the aqueous phase was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to afford *tert*-butyl 4-(cyanomethyl)-4-hydroxypiperidine-1-carboxylate which was used as such in the next step.

[00620] *Step 2: 2-(4-hydroxy-4-piperidyl)acetonitrile hydrochloride*

[00621] *tert*-Butyl 4-(cyanomethyl)-4-hydroxypiperidine-1-carboxylate (226 mg, 0.94 mmol, 1 equiv) was dissolved in dioxane (2.5 mL). 4 M HCl in dioxane (1.41 mL, 1.88 mmol, 6 equiv) was added, and the solution was stirred at RT for 5 days. The reaction mixture was concentrated under reduced pressure. The titled compound was used as such without any further purification.

Synthesis of AMI10: 4-methoxy-1,4'-bipiperidine



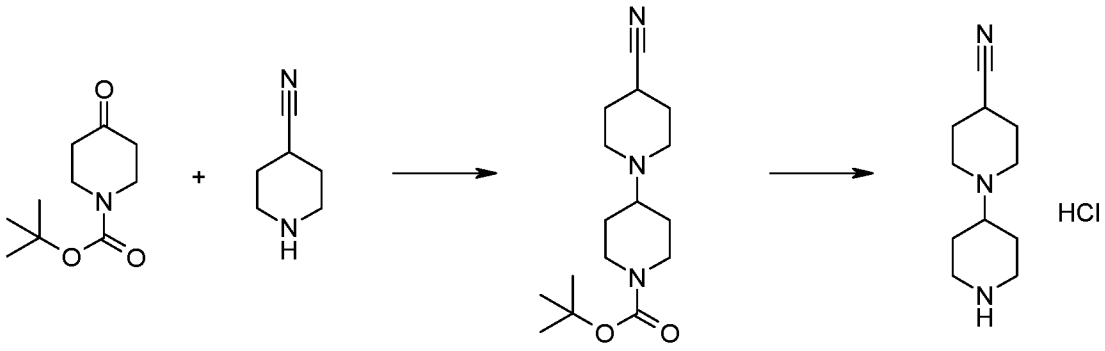
[00622] *Step 1: benzyl 4-methoxy-[1,4'-bipiperidine]-1'-carboxylate*

[00623] To a solution of benzyl 4-oxopiperidine-1-carboxylate ([19099-93-5], 40 gram, 171 mmol) and 4-methoxypiperidine ([4045-24-3], 24.6 gram) in dichloromethane (800 mL) was added acetic acid (10.8 mL, 189 mmol) and sodium triacetoxyborohydride (54.5 gram, 257 mmol). The mixture was stirred at 0 °C for 120 minutes. Next, the mixture was washed with a saturated aqueous K_2CO_3 solution. The organic phase was separated and concentrated to give a residue that was purified by chromatography on silica gel using a gradient elution with CH_2Cl_2 to CH_2Cl_2/CH_3OH (100/0 to 97/2.5) to give the titled compound.

[00624] *Step 2: 4-methoxy-1,4'-bipiperidine*

[00625] Benzyl 4-methoxy-[1,4'-bipiperidine]-1'-carboxylate (23 gram, 69 mmol) was dissolved in CH_3OH (350 mL). The solution was flushed with N_2 and 10% Pd/C (7.3 gram, 6.9 mmol) was added. After applying a balloon with H_2, the mixture was stirred at ambient temperature overnight. Next, the mixture was filtered through diatomaceous earth, and the resulting filtrate was concentrated to give the titled compound.

Synthesis of AMI11: 1-piperidin-1-ium-4-ylpiperidine-4-carbonitrile chloride



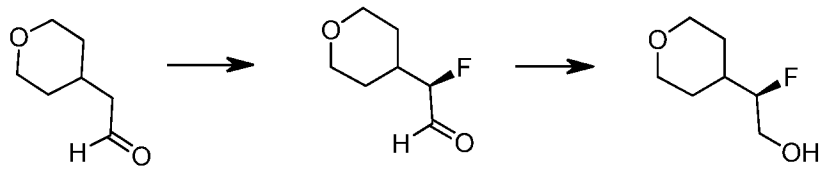
[00626] *Step 1: tert-butyl 4-(4-cyano-1-piperidyl)piperidine-1-carboxylate*

[00627] A suspension of 4-cyanopiperidine ([4395-98-6], 500 mg, 4.5 mmol), *tert*-butyl 4-oxopiperidine-1-carboxylate ([79099-07-3], 900 mg, 4.5 mmol) and AcOH (0.27 mL) in DCM (66 mL) was cooled at 0 °C. Next, sodium triacetoxyborohydride ([56553-60-7], 955 mg, 4.5 mmol) was added portion wise. After overnight stirring, the reaction was diluted with 60 mL of water together with a 1 N citric acid solution to bring down the pH till 3-4. The organic layer was separated and discarded. Next, the aqueous layer was brought to neutral pH with a saturated aqueous $NaHCO_3$ solution. After extraction with DCM, the organic phase was concentrated to give the titled compound.

[00628] *Step 2: 1-piperidin-1-ium-4-ylpiperidine-4-carbonitrile chloride*

[00629] *tert*-Butyl 4-(4-cyano-1-piperidyl)piperidine-1-carboxylate (662 mg, 2.26 mmol) was dissolved in DCM and trifluoroacetic acid ([76-05-1], 0.93 mL) was added. After overnight stirring, the mixture was concentrated to dryness. The obtained residue was suspended in 4 N HCl in dioxane. The addition of ethanol gave a suspension which was filtered to give the titled compound as a precipitate.

Synthesis of ALC02: (2R)-2-fluoro-2-tetrahydropyran-4-yl-ethanol



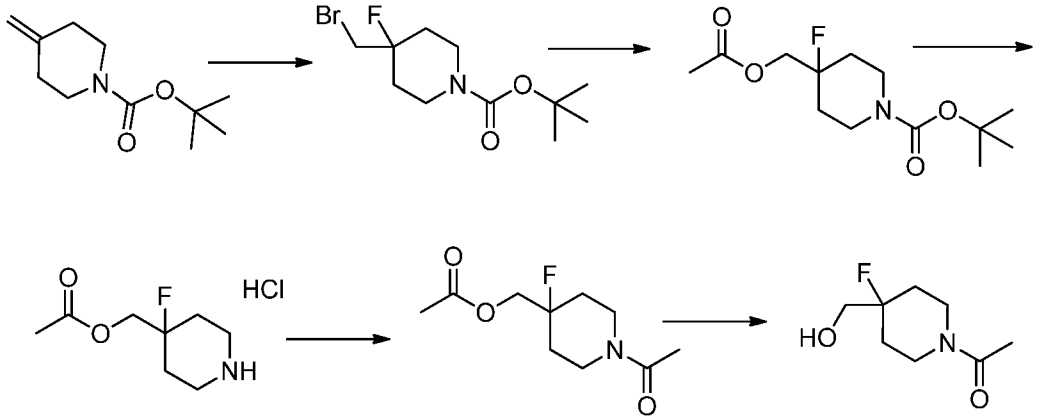
[00630] *Step 1: (2R)-2-fluoro-2-tetrahydropyran-4-yl-acetaldehyde*

[00631] To a mixture of (*R*)-5-benzyl-2,2,3-trimethylimidazolidin-4-one dichloroacetic acid salt (CAS 857303-87-8, 2.71 g, 7.80 mmol, 0.2 equiv) and *N*-fluoro-*N*-(phenylsulfonyl)benzenesulfonamide (CAS 133745-75-2, 12.30 g, 39 mmol, 1.0 equiv) in THF (200 mL) and isopropyl alcohol (25 mL) was slowly added at -20 °C a solution 2-(tetrahydro-2*H*-pyran-4-yl)acetaldehyde (5 g, 39 mmol, CAS 65626-23-5) in THF (25 mL). The mixture was stirred at –20 °C for 12 hours, then diluted with hexane (800 mL) cooled to -78 °C and filtered through silica, washed with hexane. The filtrate was concentrated to give (*R*)-2-fluoro-2-(tetrahydro-2*H*-pyran-4-yl)acetaldehyde.

[00632] *Step 2: (2R)-2-fluoro-2-tetrahydropyran-4-yl-ethanol*

[00633] To a solution of (*R*)-2-fluoro-2-(tetrahydro-2*H*-pyran-4-yl)acetaldehyde (4 g, 27.4 mmol) in dichloromethane (48 mL) and ethanol (40 mL) was added sodium borohydride (CAS 16940-66-2, 2.59 g, 68.4 mmol, 2.5 equiv). The mixture was stirred at 25 °C for 12 hours, then diluted with water and extracted with dichloromethane. The organic layer was dried, filtered, concentrated and purified by chromatography (petroleum ether, ethylate) to give (2*R*)-2-fluoro-2-tetrahydropyran-4-yl-ethanol.

Synthesis of ALC03: 1-[4-fluoro-4-(hydroxymethyl)-1-piperidyl]ethanone



[00634] *Step 1: tert-butyl 4-(bromomethyl)-4-fluoropiperidine-1-carboxylate*

[00635] To a mixture of *tert*-butyl 4-methylenepiperidine-1-carboxylate (159635-49-1, 50 g, 253 mmol) and triethylamine trihydrofluoride (102 g, 634 mmol) in dichloromethane (1 L) was added 1-bromopyrrolidine-2,5-dione (67.7 g, 380 mmol) at 0 °C. After 15 min, stirring was continued at 20 °C for 3 h. Then the mixture was poured into ice-water, neutralized with aqueous 28% ammonia and extracted with dichloromethane. The combined extracts were washed with ~0.1 N HCl and with 5% aqueous sodium hydrogencarbonate solution, dried with sodium sulfate, filtered and concentrated. The residue was purified by column chromatography to provide *tert*-butyl 4-(bromomethyl)-4-fluoropiperidine-1-carboxylate (60.1 g, 203 mmol, 80% yield).

[00636] *Step 2*: *tert-butyl 4-(acetoxymethyl)-4-fluoropiperidine-1-carboxylate*

[00637] To a mixture of *tert*-butyl 4-(bromomethyl)-4-fluoropiperidine-1-carboxylate (50 g, 169 mmol) and potassium iodide (7.01 g, 42.2 mmol) in dimethyl formamide (1.5 L) was added potassium acetate (249 g, 2532 mmol) at room temperature. The mixture was stirred at 120-140 °C for 12 h, then cooled, diluted with water, and extracted with ethyl acetate. The combined organic phases were washed with water and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by chromatography on a silica gel column eluted with hexanes:ethyl acetate to give *tert*-butyl 4-(acetoxymethyl)-4-fluoropiperidine-1-carboxylate (42 g, 153 mmol, 90% yield).

[00638] *Step 3*: *(4-fluoropiperidin-4-yl)methyl acetate hydrochloride*

[00639] To a mixture of *tert*-butyl 4-(acetoxymethyl)-4-fluoropiperidine-1-carboxylate (50 g, 182 mmol) in ethyl acetate (400 mL) was added a solution of HCl (1 L) at 0 °C. The mixture was allowed to warm to 15 °C and stirred at 15 °C overnight. The reaction mixture was concentrated under vacuum, and the residue washed with dichloromethane. Then the precipitate was collected by filtration to obtain (4-fluoropiperidin-4-yl)methyl acetate hydrochloride (33 g, 156 mmol, 86% yield).

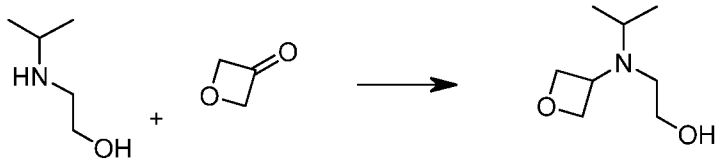
[00640] *Step 4: (1-acetyl-4-fluoropiperidin-4-yl)methyl acetate*

[00641] To a solution of (4-fluoropiperidin-4-yl)methyl acetate hydrochloride (30 g, 142 mmol) and triethylamine (59.3 mL, 425 mmol) in dichloromethane (300 mL) was added acetyl chloride (16.69 g, 213 mmol) at 0 °C. The mixture was stirred overnight at 20 °C, then diluted with dichloromethane and washed with water. The dichloromethane layer was concentrated to give crude (1-acetyl-4-fluoropiperidin-4-yl)methyl acetate (21 g, 97 mmol, 68.2% yield).

[00642] *Step 5: 1-[4-fluoro-4-(hydroxymethyl)-1-piperidyl]ethanone*

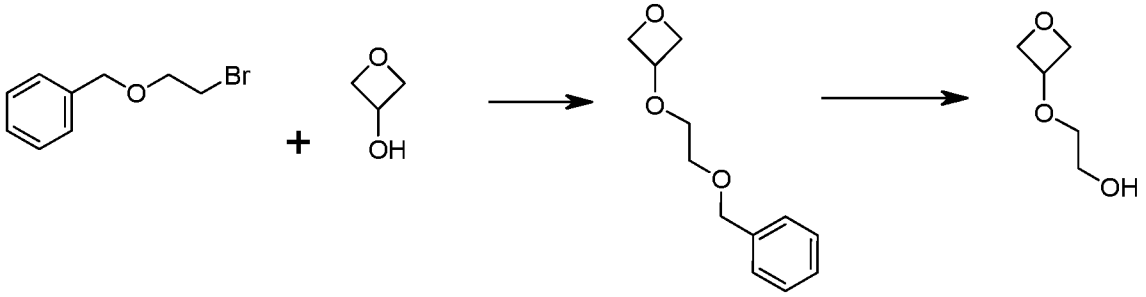
[00643] (1-Acetyl-4-fluoropiperidin-4-yl)methyl acetate (30.8 g, 142 mmol) was dissolved in 3:1 THF:water (400 mL) at 0 °C, and then lithium hydroxide (6.80 g, 284 mmol) was added in one portion. The reaction mixture was stirred for 1 hour at 0 °C. The mixture was poured into ethyl acetate and water, shaken, and the layers separated. The aqueous layer was extracted with ethyl acetate. The ethyl acetate extracts were combined, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was titrated with CH_2Cl_2 and cyclohexane to afford 1-[4-fluoro-4-(hydroxymethyl)-1-piperidyl]ethanone (19 g, 108 mmol, 76% yield). Alternatively, 1-[4-fluoro-4-(hydroxymethyl)-1-piperidyl]ethanone is available by treatment of commercially available (4-fluoropiperidin-4-yl)methanol (CAS: 949100-11-2) with acetic anhydride.

Synthesis of ALC04: 2-[isopropyl(oxetan-3-yl)amino]ethanol



[00644] 2-[Isopropyl(oxetan-3-yl)amino]ethanol is available by the reaction of (isopropylamino)ethanol (CAS: 109-56-8) with 1 equivalent of 3-oxetanone (CAS: 6704-31-0) in a solvent such as isopropanol or THF with a reducing agent such as sodium borohydride or sodium triacetoxyborohydride, followed by distillation.

Synthesis of ALC05: 2-(oxetan-3-yloxy)ethanol



[00645] *Step 1: 3-(2-benzyloxyethoxy)oxetane*

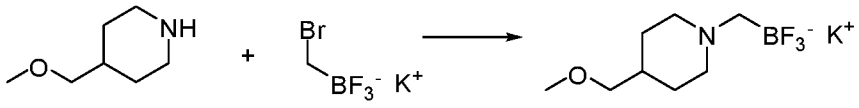
[00646] 1.0 M Lithium bis(trimethylsilyl)amide in THF (31.1 mL, 31.1 mmol, 1.2 equiv) was added dropwise at RT to a solution of oxetan-3-ol (1.92 g, 25.9 mmol) and ((2-

bromoethoxy)methyl)benzene (6.13 g, 28.5 mmol, 1.1 equiv) in dioxane (15 mL). The mixture was stirred at ambient temperature for 2 hours. DMF (20 mL) was added along with sodium iodide, and the reaction mixture was stirred at ambient temperature overnight, then stirred at 70 ^{o}C for 20 hours. The reaction mixture was concentrated under reduced pressure, and the residue was partitioned between ethyl acetate and aqueous citric acid. The organic layer was washed twice with brine, then dried over $MgSO_4$, filtered and concentrated. The residue was purified by column chromatography on silica gel (dichloromethane and ethyl acetate) to give 3-(2-(benzyloxy)ethoxy)oxetane.

[00647] *Step 2: 2-(oxetan-3-yloxy)ethanol*

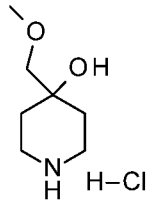
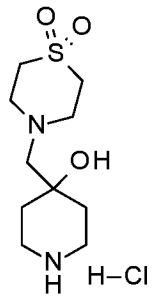
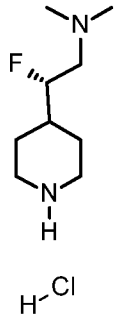
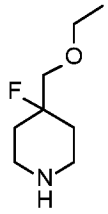
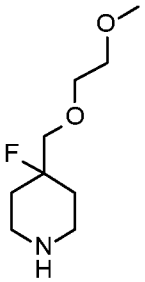
[00648] To a solution of 3-(2-(benzyloxy)ethoxy)oxetane (1.40 g, 6.72 mmol) in THF (28 mL) was added 20% palladium hydroxide on carbon (0.178 g, 0.645 mmol) in a 50 mL pressure bottle, and the mixture was stirred for 4 h under a hydrogen atmosphere. The reaction mixture was filtered free of catalyst and solids, and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel chromatography eluting with a mixture of ethyl acetate and dichloromethane to give the titled compound.

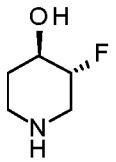
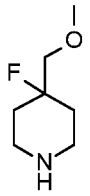
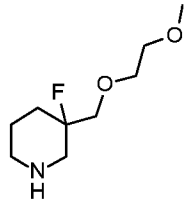
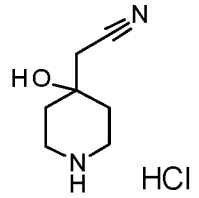
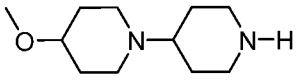
Synthesis of intermediate BF01: potassium trifluorido{[4-(methoxymethyl)piperidin-1-yl]methyl}borate



[00649] 4-(Methoxymethyl)piperidine hydrochloride ([916317-00-5], 1.0 g, 6.03 mmol,), potassium bromomethyl trifluoroborate (1.21 g, 6.03 mmol), $KHCO_3$ (1.2 g, 12.1 mmol) and KI (100 mg, 0.6 mmol) were stirred under N_2 in dry THF (8 mL) at 80 °C for 4 hours. The reaction mixture was cooled to room temperature and concentrated in vacuo. The residue was suspended in dry acetone and filtered. The filtrate was treated with diethyl ether, and the resulting precipitate was collected by filtration and dried to afford the titled compound, which was used as such in the next step.

Table IX. List of amines

Int.	Structure	Name	SM	method	MW	Mes
AMI01		4-(methoxymethyl)piperidin-4-ol hydrochloride	14780 4-30-6	Specific example	181	
AMI02		4-[(1,1-dioxo-1,4-thiazinan-4-yl)methyl]piperidin-4-ol hydrochloride	14780 4-30-6	Specific example	284	
AMI03		(2*S*)-2-fluoro-*N*,*N*-dimethyl-2-(4-piperidyl)ethanamine hydrochloride	14237 4-19-4	Specific example	210	
AMI04		4-(ethoxymethyl)-4-fluoro-piperidine	14285 1-03-4	Specific example	161	
AMI05		4-fluoro-4-(2-methoxyethoxymethyl)piperidine	61473 0-97-1	Specific example	191	

AMI06 955082-95-8 or 955028-84-9 (HCl salt)		(3*R*,4*R*)-3-fluoropiperidin-4-ol			119	
AMI07		4-fluoro-4-(methoxymethyl)piperidine	614730-97-1	Specific example	147	
AMI08		3-fluoro-3-(2-methoxyethoxymethyl)piperidine	1209781-11-2	Specific example	191	
AMI09		2-(4-hydroxy-4-piperidyl)acetonitrile hydrochloride	79099-07-3	Specific example	140	
AMI10		4-methoxy-1,4'-bipiperidine	19099-93-5 and 4045-24-3	Specific example	198	

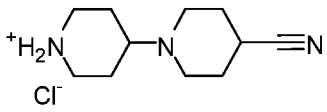
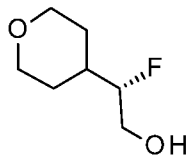
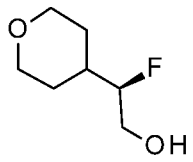
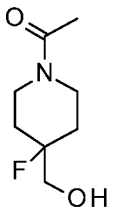
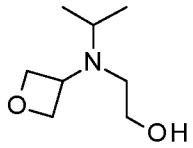
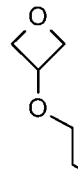
AMI11		1-piperidin-1-ium-4-ylpiperidine-4-carbonitrile chloride	79099-07-3 and 4395-98-6	Specific example	249	

Table X. List of alcohols

Int.	Structure	Name	SM	method	MW	Mes
ALC01		(2*S*)-2-fluoro-2-tetrahydropyran-4-yl-ethanol		Analogous to ALC02	148	
ALC02		(2*R*)-2-fluoro-2-tetrahydropyran-4-yl-ethanol	65626-23-5	Specific example	148	
ALC03		1-[4-fluoro-4-(hydroxymethyl)-1-piperidyl]ethanone	159635-49-1	Specific example	175	
ALC04		2-[isopropyl(oxetan-3-yl)amino]ethanol		Specific example	159	
ALC05		2-(oxetan-3-yloxy)ethanol		Specific example	118	

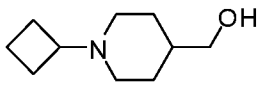
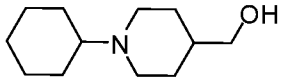
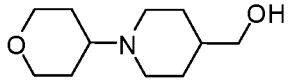
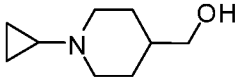
Int.	Structure	Name	SM	method	MW	Mes
ALC06		(1-cyclobutyl-4-piperidyl)methanol	6457-49-4 and 1191-95-3	I18	169	170
ALC07		(1-cyclohexyl-4-piperidyl)methanol	6457-49-4 and 108-94-1	I18	197	198
ALC08		(1-tetrahydropyran-4-yl-4-piperidyl)methanol	6457-49-4 and 29943-42-8	I18	199	200
ALC09		(1-cyclopropyl-4-piperidyl)methanol	6457-49-4 and 27374-25-0	I26	155	156

Table XI. List of BF_3 salts

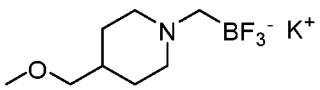
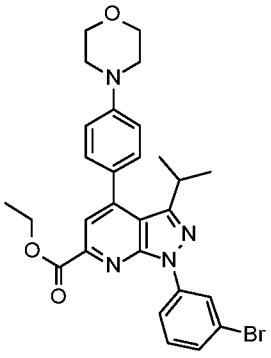
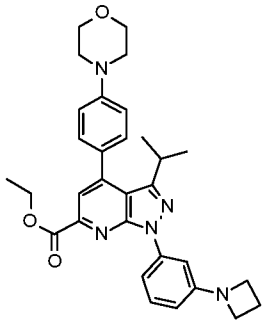
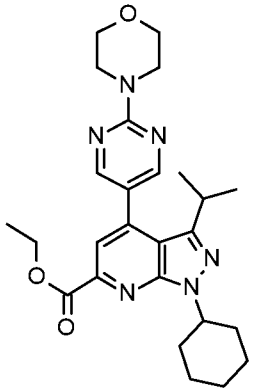
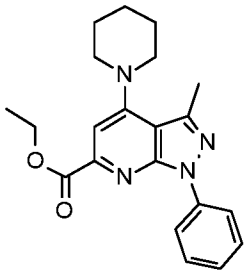
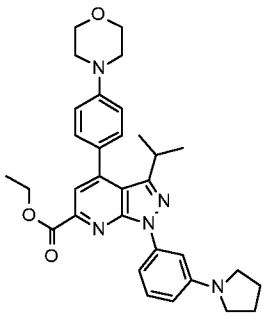
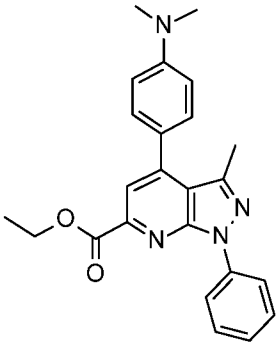
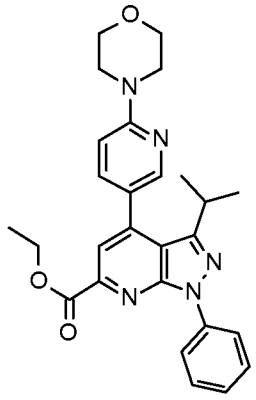
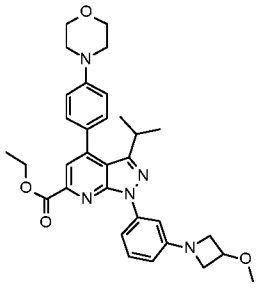
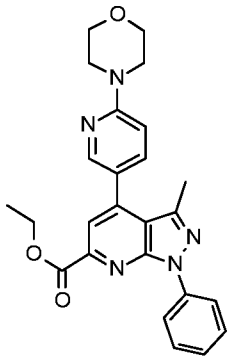
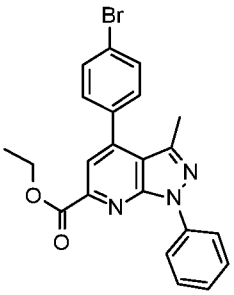
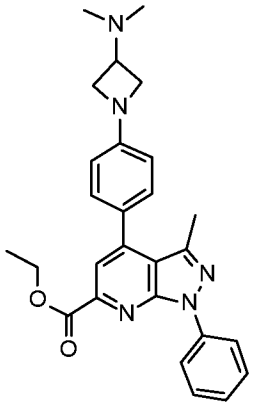
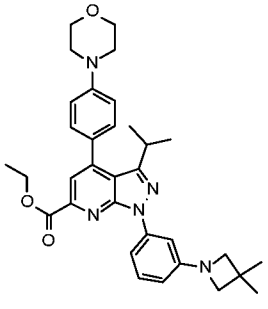
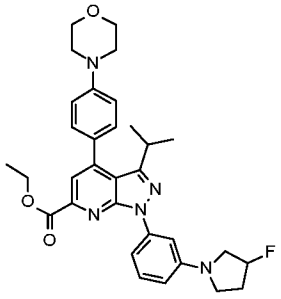
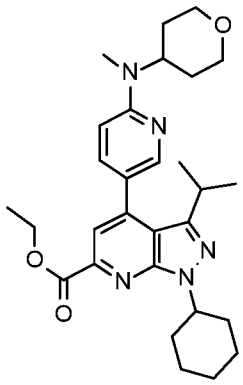
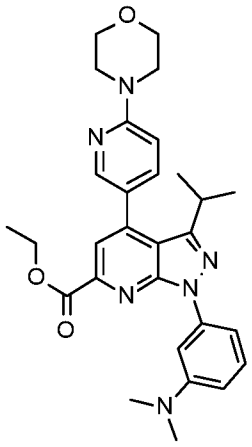
Int.	Structure	Name	SM	method	MW	Mes
BF01		potassium trifluorido{[4-(methoxymethyl)piperidin-1-yl]methyl}borate	916317-00-5 and 888711-44-2	Specific example	249	NA

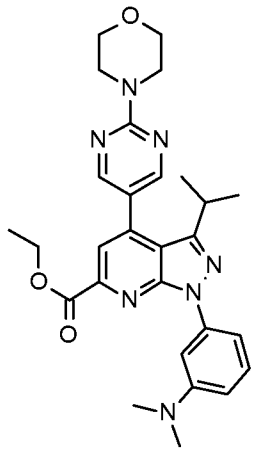
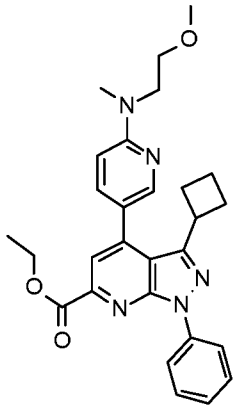
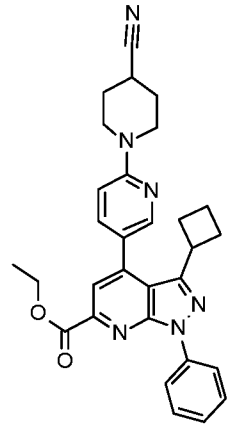
Table XII. List of esters

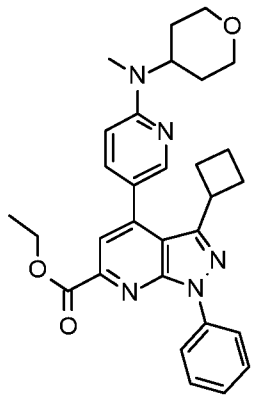
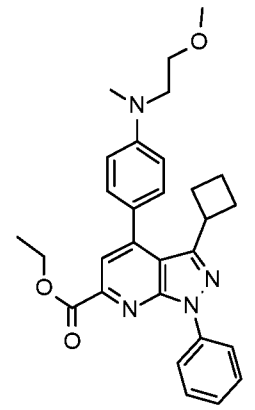
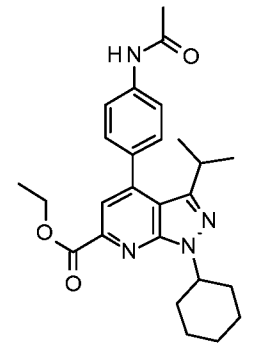
Int.	Structure	Name	SM	method	MW	Mes
E001		ethyl 1-(3-bromophenyl)-3-isopropyl-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	A242	I9, Specific example	548-550	549-551
E002		ethyl 1-[3-(azetidin-1-yl)phenyl]-3-isopropyl-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	E001, 935670-07-8	I8, Specific example	525	526
E003		ethyl 1-cyclohexyl-3-isopropyl-4-(2-morpholinopyrimidin-5-yl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP22, AMP23	I1	478	479
E004		ethyl 3-methyl-1-phenyl-4-(1-piperidyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP13, 98-77-1	I3	364	365

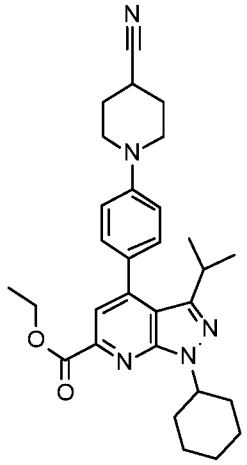
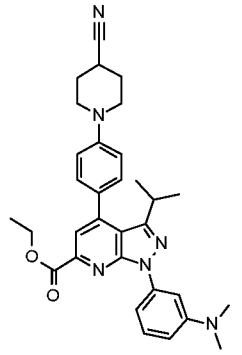
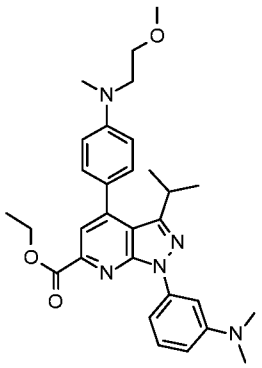
Int.	Structure	Name	SM	method	MW	Mes
E005		ethyl 3-isopropyl-4-(4-morpholinophenyl)-1-(3-pyrrolidin-1-ylphenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	E001	I8	539	540
E006		ethyl 4-[4-(dimethylamino)phenyl]-3-methyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP25, 1131-18-6	I1	400	401
E007		ethyl 3-isopropyl-4-(6-morpholino-3-pyridyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP26, AMP04	I1	471	472
E008		ethyl 3-isopropyl-1-[3-(3-methoxyazetidin-1-yl)phenyl]-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	E001, 110925-17-2	I8, Specific example	555	556

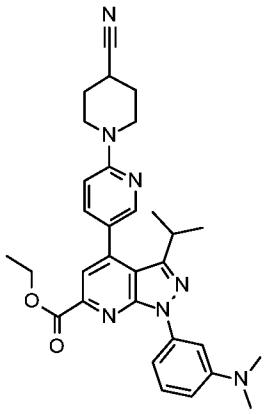
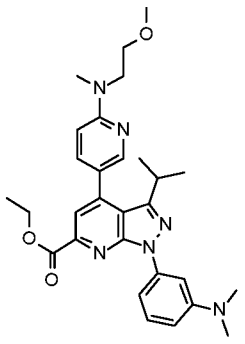
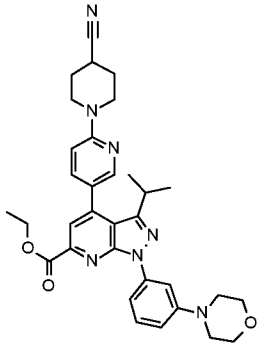
Int.	Structure	Name	SM	method	MW	Mes
E009		ethyl 3-methyl-4-(6-morpholino-3-pyridyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP26, 1131-18-6	I1	443	444
E010		ethyl 4-(4-bromophenyl)-3-methyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	A246	I9	435-437	436-438
E011		ethyl 4-[4-[3-(dimethylamino)azetidin-1-yl]phenyl]-3-methyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E010, 138022-85-2	I10, Specific example	455	456
E012		ethyl 1-[3-(3,3-dimethylazetidin-1-yl)phenyl]-3-isopropyl-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	E001, 19816-92-3	I8	553	554

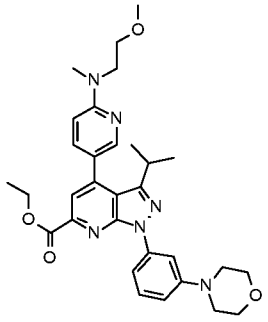
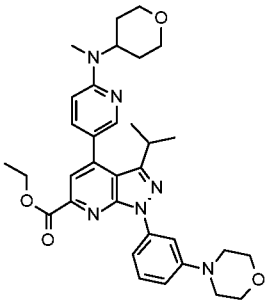
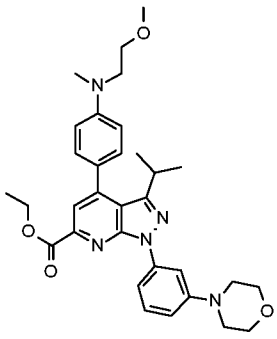
Int.	Structure	Name	SM	method	MW	Mes
E013		ethyl 1-[3-(3-fluoropyrrolidin-1-yl)phenyl]-3-isopropyl-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	E001, 116574-74-4	I8	553	558
E014		ethyl 1-cyclohexyl-3-isopropyl-4-[6-[methyl(tetrahydropyran-4-yl)amino]-3-pyridyl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP10, AMP23	I1	505	506
E015		ethyl 1-[3-(dimethylamino)phenyl]-3-isopropyl-4-(6-morpholino-3-pyridyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP26, AMP06	I1	514	515

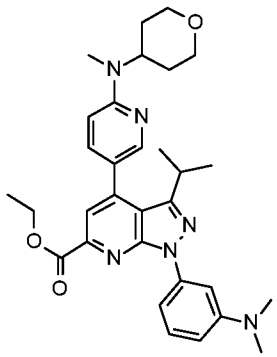
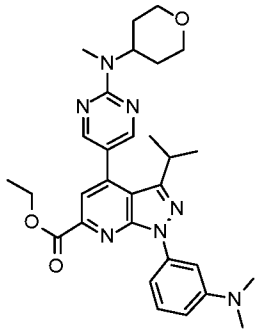
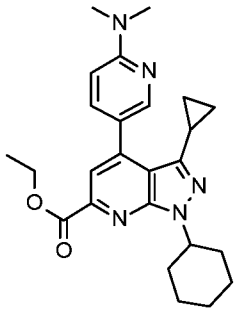
Int.	Structure	Name	SM	method	MW	Mes
E016		ethyl 1-[3-(dimethylamino)phenyl]-3-isopropyl-4-(2-morpholinopyrimidin-5-yl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP22, AMP06	I1	515	516
E017		ethyl 3-cyclobutyl-4-[6-[2-methoxyethyl(methyl)amino]-3-pyridyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP08, AMP29	I1	485	486
E018		ethyl 4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP09, AMP29	I1	506	507

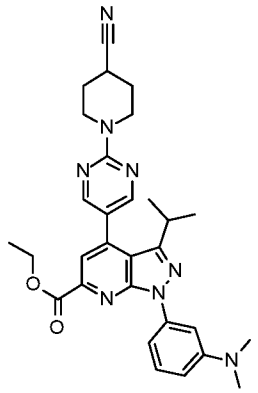
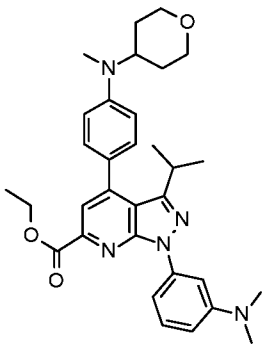
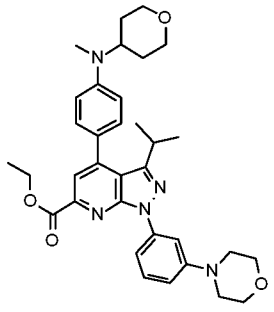
Int.	Structure	Name	SM	method	MW	Mes
E019		ethyl 3-cyclobutyl-4-[6-[methyl(tetrahydropyran-4-yl)amino]-3-pyridyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP10, AMP29	I1	511	512
E020		ethyl 3-cyclobutyl-4-[4-[2-methoxyethyl(methyl)amino]phenyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP11, AMP29	I1	484	485
E021		ethyl 4-(4-acetamidophenyl)-1-cyclohexyl-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP24, AMP23	I1	448	449

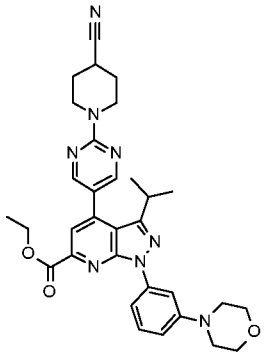
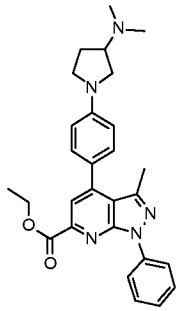
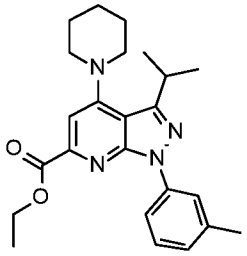
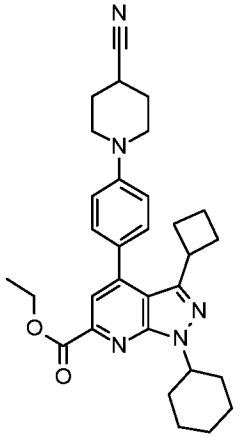
Int.	Structure	Name	SM	method	MW	Mes
E022		ethyl 4-[4-(4-cyano-1-piperidyl)phenyl]-1-cyclohexyl-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP12, AMP23	I1	499	500
E023		ethyl 4-[4-(4-cyano-1-piperidyl)phenyl]-1-[3-(dimethylamino)phenyl]-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP12, AMP06	I1	536	537
E024		ethyl 1-[3-(dimethylamino)phenyl]-3-isopropyl-4-[4-[2-methoxyethyl(methyl)amino]phenyl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP11, AMP06	I1	515	516

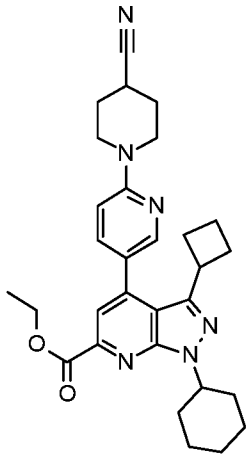
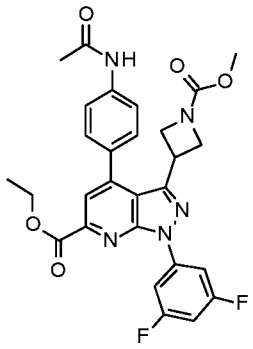
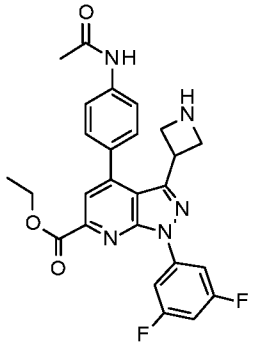
Int.	Structure	Name	SM	method	MW	Mes
E025		ethyl 4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-1-[3-(dimethylamino)phenyl]-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP09, AMP06	I1	537	538
E026		ethyl 1-[3-(dimethylamino)phenyl]-3-isopropyl-4-[6-[2-methoxyethyl(methyl)amino]-3-pyridyl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP08, AMP06	I1	516	517
E027		ethyl 4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-isopropyl-1-(3-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP09, AMP10	I1	579	580

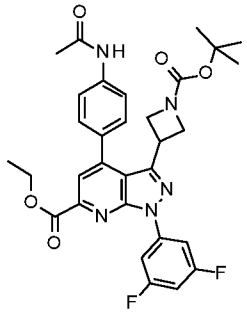
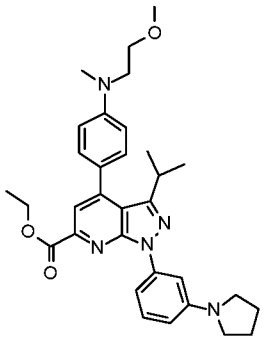
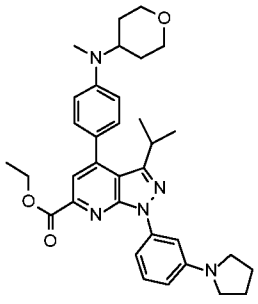
Int.	Structure	Name	SM	method	MW	Mes
E028		ethyl 3-isopropyl-4-[6-[2-methoxyethyl(methyl)amino]-3-pyridyl]-1-(3-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP08, AMP10	I1	558	559
E029		ethyl 3-isopropyl-4-[6-[methyl(tetrahydropyran-4-yl)amino]-3-pyridyl]-1-(3-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP10, AMP10	I1	584	585
E030		ethyl 3-isopropyl-4-[4-[2-methoxyethyl(methyl)amino]phenyl]-1-(3-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP11, AMP10	I1	557	558

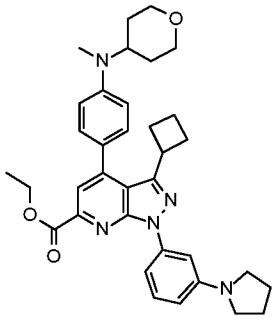
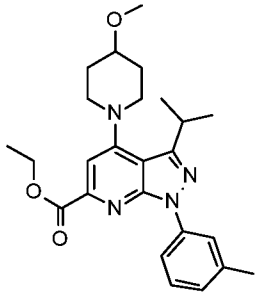
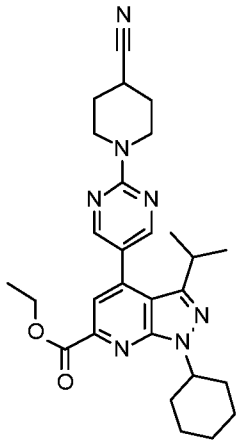
Int.	Structure	Name	SM	method	MW	Mes
E031		ethyl 1-[3-(dimethylamino)phenyl]-3-isopropyl-4-[6-[methyl(tetrahydropyran-4-yl)amino]-3-pyridyl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP10, AMP06	I1	542	543
E032		ethyl 1-[3-(dimethylamino)phenyl]-3-isopropyl-4-[2-[methyl(tetrahydropyran-4-yl)amino]pyrimidin-5-yl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP13, AMP06	I1	543	544
E033		ethyl 1-cyclohexyl-3-cyclopropyl-4-[6-(dimethylamino)-3-pyridyl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP20, AMP39	I1	433	434

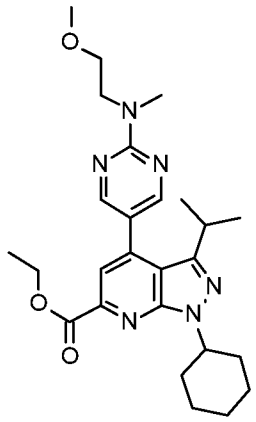
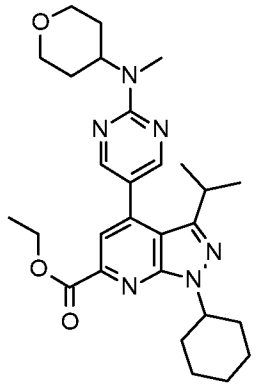
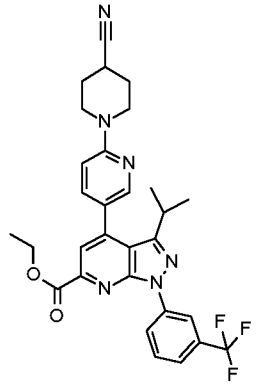
Int.	Structure	Name	SM	method	MW	Mes
E034		ethyl 4-[2-(4-cyano-1-piperidyl)pyrimidin-5-yl]-1-[3-(dimethylamino)phenyl]-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP14, AMP06	I1	538	539
E035		ethyl 1-[3-(dimethylamino)phenyl]-3-isopropyl-4-[4-[methyl(tetrahydropyran-4-yl)amino]phenyl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP15, AMP06	I1	541	542
E036		ethyl 3-isopropyl-4-[4-[methyl(tetrahydropyran-4-yl)amino]phenyl]-1-(3-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP15, AMP10	I1	583	584

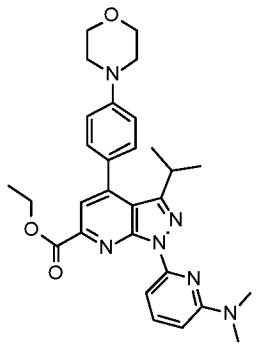
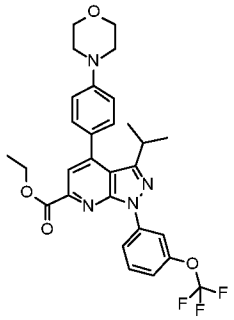
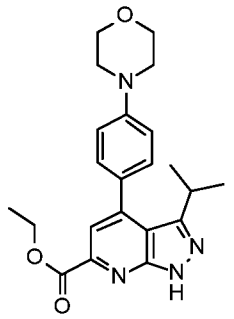
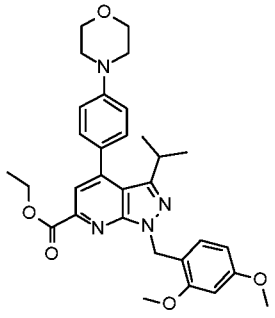
Int.	Structure	Name	SM	method	MW	Mes
E037		ethyl 4-[2-(4-cyano-1-piperidyl)pyrimidin-5-yl]-3-isopropyl-1-(3-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP14, AMP10	I1	580	581
E038		ethyl 4-[4-[3-(dimethylamino)pyrrolidin-1-yl]phenyl]-3-methyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E010, 69478-75-7	I10	469	470
E039		ethyl 3-isopropyl-1-(*m*-tolyl)-4-(1-piperidyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP01, 98-77-1	I3	406	407
E040		ethyl 4-[4-(4-cyano-1-piperidyl)phenyl]-3-cyclobutyl-1-cyclohexyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP12, AMP35	I1	511	512

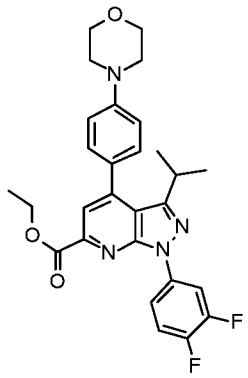
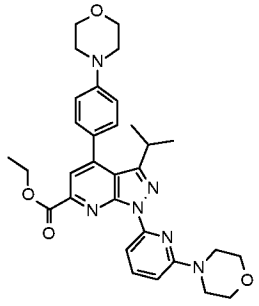
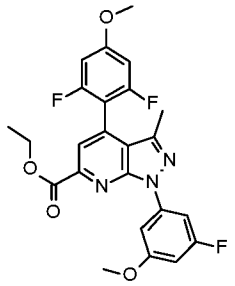
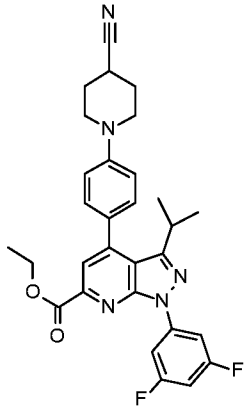
Int.	Structure	Name	SM	method	MW	Mes
E041		ethyl 4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-cyclobutyl-1-cyclohexyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP09, AMP35	I1	512	513
E042		ethyl 4-(4-acetamidophenyl)-1-(3,5-difluorophenyl)-3-(1-methoxycarbonylazetidin-3-yl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	E043	I11, Specific example	549	550
E043		ethyl 4-(4-acetamidophenyl)-3-(azetidin-3-yl)-1-(3,5-difluorophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	E044	Specific example	491	492

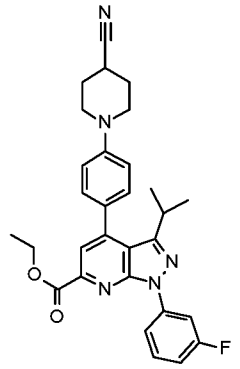
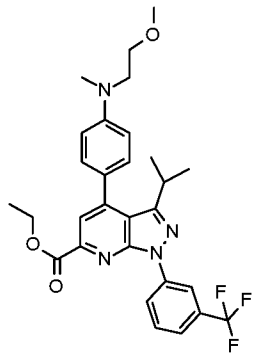
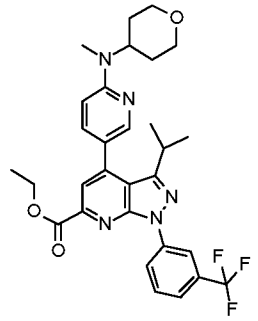
Int.	Structure	Name	SM	method	MW	Mes
E044		ethyl 4-(4-acetamidophenyl)-3-(1-*tert*-butoxycarbonylazetidin-3-yl)-1-(3,5-difluorophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP24, AMP40	I1	591	592
E045		ethyl 3-isopropyl-4-[4-[2-methoxyethyl(methyl)amino]phenyl]-1-(3-pyrrolidin-1-ylphenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP11, AMP11	I1	541	542
E046		ethyl 3-isopropyl-4-[4-[methyl(tetrahydropyran-4-yl)amino]phenyl]-1-(3-pyrrolidin-1-ylphenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP15, AMP11	I1	567	568

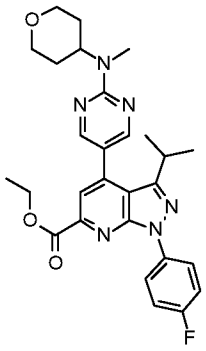
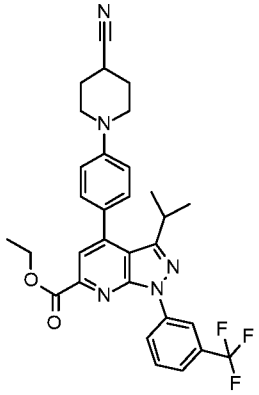
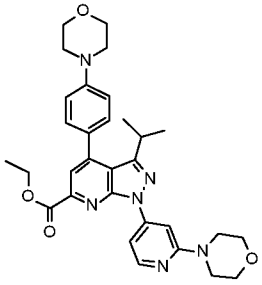
Int.	Structure	Name	SM	method	MW	Mes
E047		ethyl 3-cyclobutyl-4-[4-[methyl(tetrahydropyran-4-yl)amino]phenyl]-1-(3-pyrrolidin-1-ylphenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP15, AMP31	I1	580	581
E048		ethyl 3-isopropyl-4-(4-methoxy-1-piperidyl)-1-(*m*-tolyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP01, 4045-24-3	I3	436	437
E049		ethyl 4-[2-(4-cyano-1-piperidyl)pyrimidin-5-yl]-1-cyclohexyl-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP14, AMP23	I1	501	502

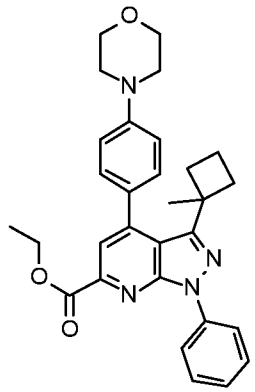
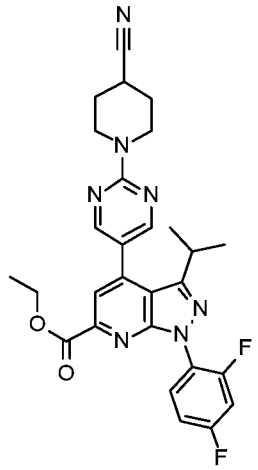
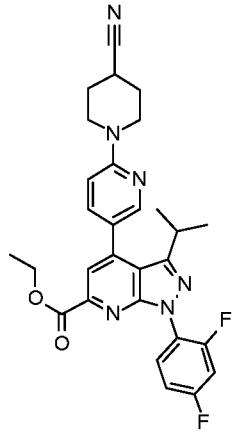
Int.	Structure	Name	SM	method	MW	Mes
E050		ethyl 1-cyclohexyl-3-isopropyl-4-[2-[2-methoxyethyl(methyl)amino]pyrimidin-5-yl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP16, AMP23	I1	480	481
E051		ethyl 1-cyclohexyl-3-isopropyl-4-[2-[methyl(tetrahydropyran-4-yl)amino]pyrimidin-5-yl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP13, AMP23	I1	506	507
E052		ethyl 4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-isopropyl-1-[3-(trifluoromethyl)phenyl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP09, AMP08	I1	562	563

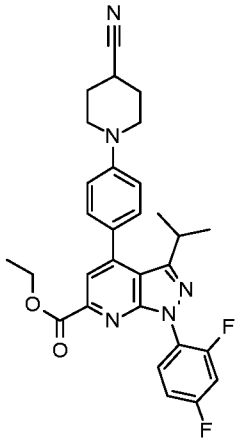
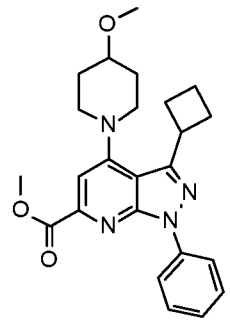
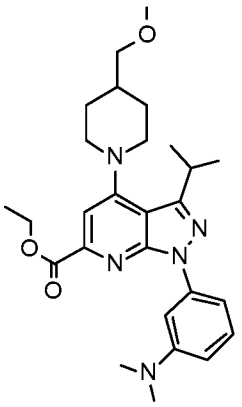
Int.	Structure	Name	SM	method	MW	Mes
E053		ethyl 1-[6-(dimethylamino)-2-pyridyl]-3-isopropyl-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP18, AMP18	I1	514	515
E054		ethyl 3-isopropyl-4-(4-morpholinophenyl)-1-[3-(trifluoromethoxy)phenyl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	E055, 179113-90-7	I4	554	555
E055		ethyl 3-isopropyl-4-(4-morpholinophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E056	I15, Specific example	394	395
E056		ethyl 1-[(2,4-dimethoxyphenyl)methyl]-3-isopropyl-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP18, AMP28	I1	544	545

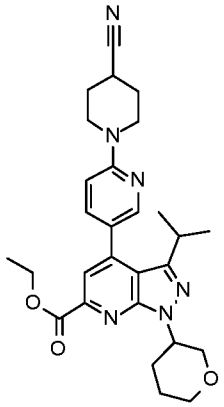
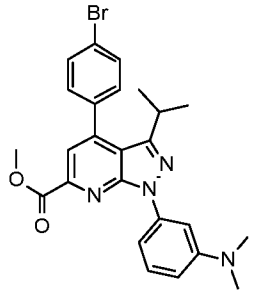
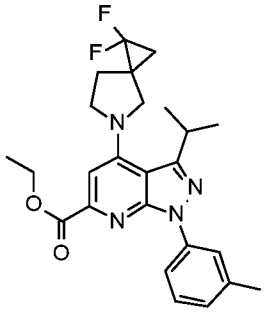
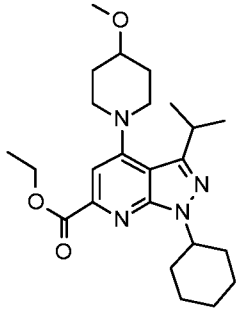
Int.	Structure	Name	SM	method	MW	Mes
E057		ethyl 1-(3,4-difluorophenyl)-3-isopropyl-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	E055	I4	506	507
E058		ethyl 3-isopropyl-4-(4-morpholinophenyl)-1-(6-morpholino-2-pyridyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP18, AMP19	I1	556	557
E059		ethyl 4-(2,6-difluoro-4-methoxy-phenyl)-1-(3-fluoro-5-methoxy-phenyl)-3-methyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP17, AMP03	I1	471	472
E060		ethyl 4-[4-(4-cyano-1-piperidyl)phenyl]-1-(3,5-difluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP12, AMP09	I1	529	530

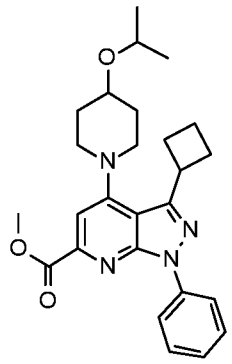
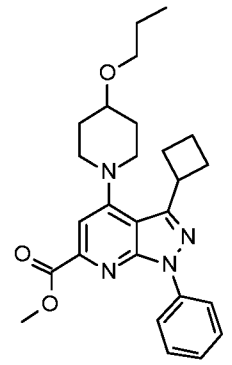
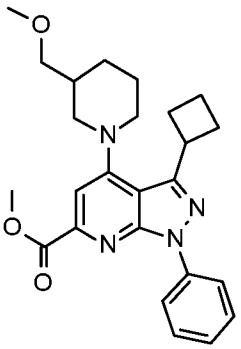
Int.	Structure	Name	SM	method	MW	Mes
E061		ethyl 4-[4-(4-cyano-1-piperidyl)phenyl]-1-(3-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP12, AMP12	I1	511	512
E062		ethyl 3-isopropyl-4-[4-[2-methoxyethyl(methyl)amino]phenyl]-1-[3-(trifluoromethyl)phenyl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP11, AMP08	I1	540	541
E063		ethyl 3-isopropyl-4-[6-[methyl(tetrahydropyran-4-yl)amino]-3-pyridyl]-1-[3-(trifluoromethyl)phenyl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP10, AMP08	I1	567	568

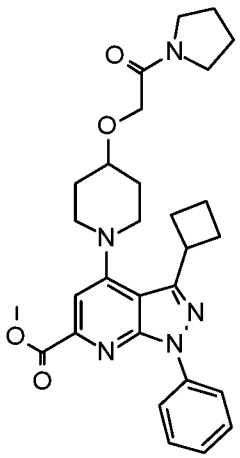
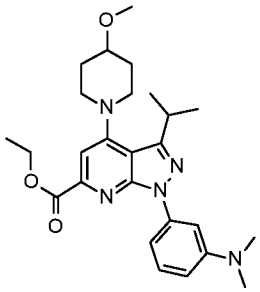
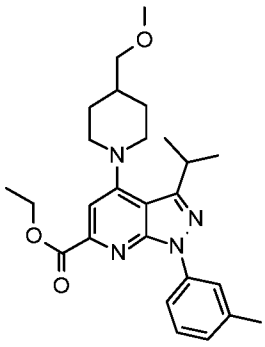
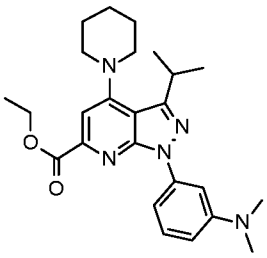
Int.	Structure	Name	SM	method	MW	Mes
E064		ethyl 1-(4-fluorophenyl)-3-isopropyl-4-[2-[methyl(tetrahydropyran-4-yl)amino]pyrimidin-5-yl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP13, AMP13	I1	518	519
E065		ethyl 4-[4-(4-cyano-1-piperidyl)phenyl]-3-isopropyl-1-[3-(trifluoromethyl)phenyl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP12, AMP08	I1	561	562
E066		ethyl 3-isopropyl-4-(4-morpholinophenyl)-1-(2-morpholino-4-pyridyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP18, AMP21	I1	556	557

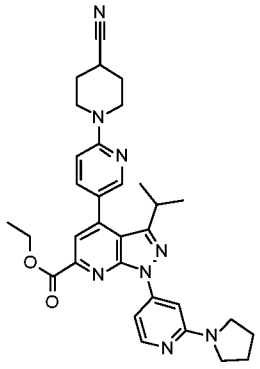
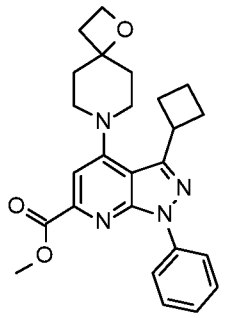
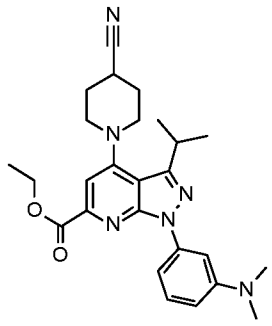
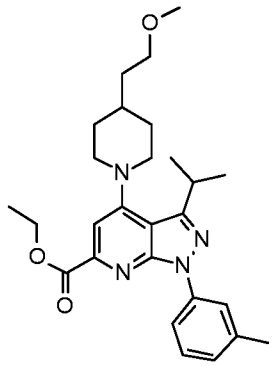
Int.	Structure	Name	SM	method	MW	Mes
E067		ethyl 3-(1-methylcyclobutyl)-4-(4-morpholinophenyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP18, AMP41	I1	496	497
E068		ethyl 4-[2-(4-cyano-1-piperidyl)pyrimidin-5-yl]-1-(2,4-difluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP14, AMP14	I1	531	532
E069		ethyl 4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-1-(2,4-difluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP09, AMP14	I1	530	531

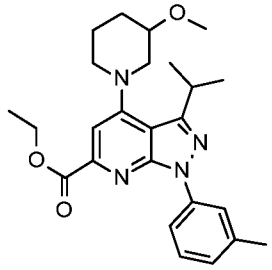
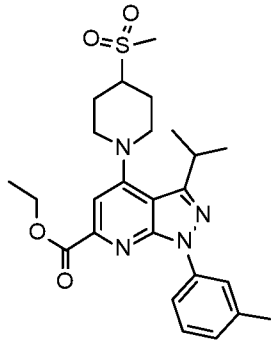
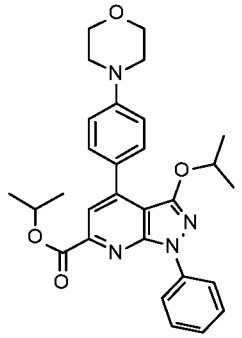
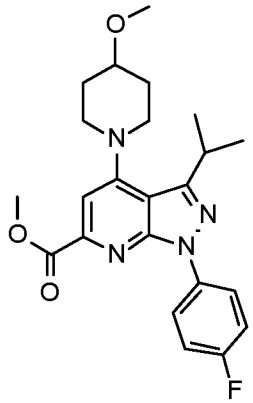
Int.	Structure	Name	SM	method	MW	Mes
E070		ethyl 4-[4-(4-cyano-1-piperidyl)phenyl]-1-(2,4-difluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP12, AMP14	I1	529	530
E071		methyl 3-cyclobutyl-4-(4-methoxy-1-piperidyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	420	421
E072		ethyl 1-[3-(dimethylamino)phenyl]-3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP03	I3	479	480

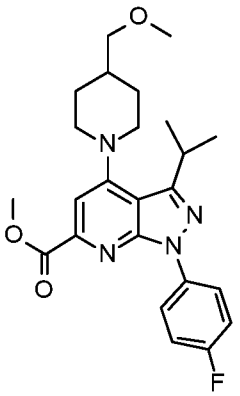
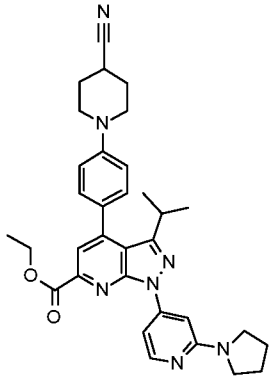
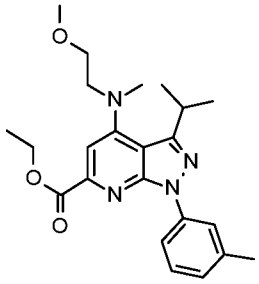
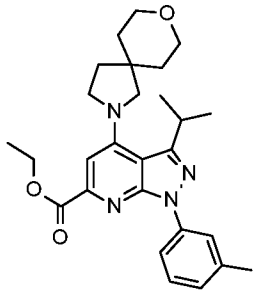
Int.	Structure	Name	SM	method	MW	Mes
E073		ethyl 4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-isopropyl-1-tetrahydropyran-3-yl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP09, AMP25	I1	502	503
E074		methyl 4-(4-bromophenyl)-1-[3-(dimethylamino)phenyl]-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	608128-34-3, AMP06	I1	492-494	493-495
E075		ethyl 4-(2,2-difluoro-5-azaspiro[2.4]heptan-5-yl)-3-isopropyl-1-(*m*-tolyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP01	I3	454	455
E076		ethyl 1-cyclohexyl-3-isopropyl-4-(4-methoxy-1-piperidyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP04	I3	428	429

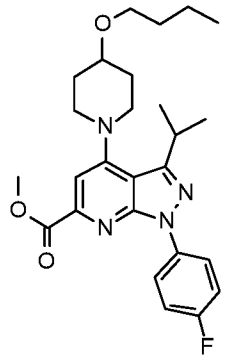
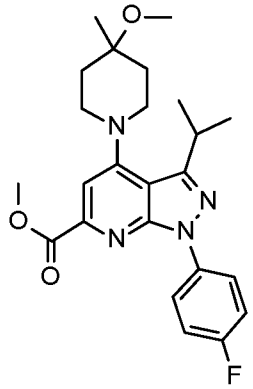
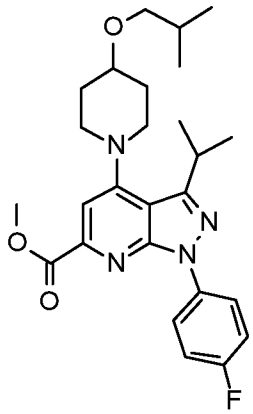
Int.	Structure	Name	SM	method	MW	Mes
E077		methyl 3-cyclobutyl-4-(4-isopropoxy-1-piperidyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	448	449
E078		methyl 3-cyclobutyl-1-phenyl-4-(4-propoxy-1-piperidyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	448	449
E079		methyl 3-cyclobutyl-4-[3-(methoxymethyl)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	434	435

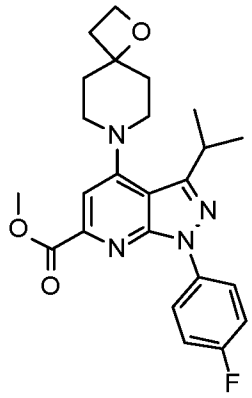
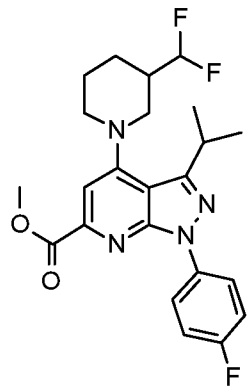
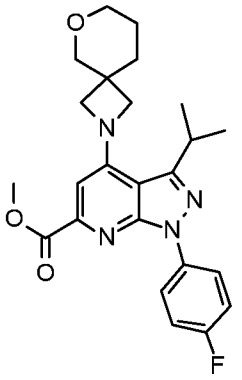
Int.	Structure	Name	SM	method	MW	Mes
E080		methyl 3-cyclobutyl-4-[4-(2-oxo-2-pyrrolidin-1-yl-ethoxy)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	517	518
E081		ethyl 1-[3-(dimethylamino)phenyl]-3-isopropyl-4-(4-methoxy-1-piperidyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP03	I3	465	466
E082		ethyl 3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]-1-(*m*-tolyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP01	I3	450	451
E083		ethyl 1-[3-(dimethylamino)phenyl]-3-isopropyl-4-(1-piperidyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP03	I3	435	436

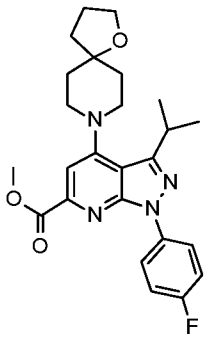
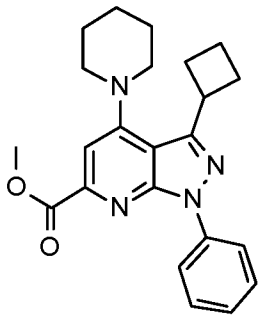
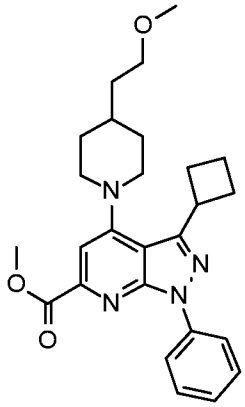
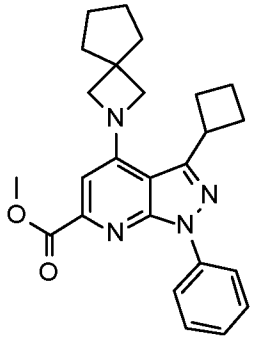
Int.	Structure	Name	SM	method	MW	Mes
E084		ethyl 4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-isopropyl-1-(2-pyrrolidin-1-yl-4-pyridyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP09, AMP22	I1	564	565
E085		methyl 3-cyclobutyl-4-(1-oxa-7-azaspiro[3.5]nonan-7-yl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	432	433
E086		ethyl 4-(4-cyano-1-piperidyl)-1-[3-(dimethylamino)phenyl]-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP03	I3	460	461
E087		ethyl 3-isopropyl-4-[4-(2-methoxyethyl)-1-piperidyl]-1-(*m*-tolyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP01	I3	464	465

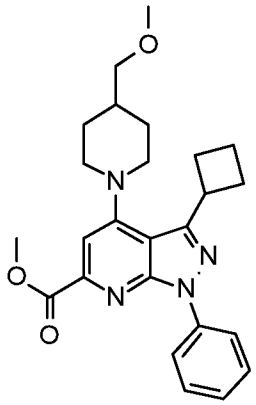
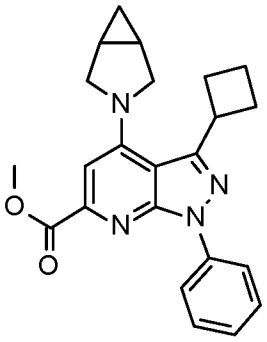
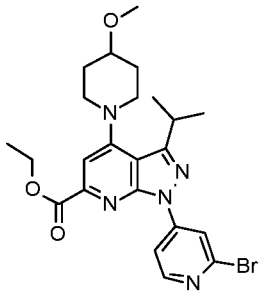
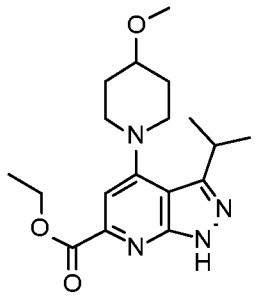
Int.	Structure	Name	SM	method	MW	Mes
E088		ethyl 3-isopropyl-4-(3-methoxy-1-piperidyl)-1-(*m*-tolyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP01	I3	436	437
E089		ethyl 3-isopropyl-4-(4-methylsulfonyl-1-piperidyl)-1-(*m*-tolyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP01	I3	484	485
E090		isopropyl 3-isopropoxy-4-(4-morpholinophenyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	A256	I17, Specific example	500	501
E091		methyl 1-(4-fluorophenyl)-3-isopropyl-4-(4-methoxy-1-piperidyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP05	I3	426	427

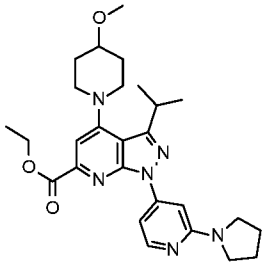
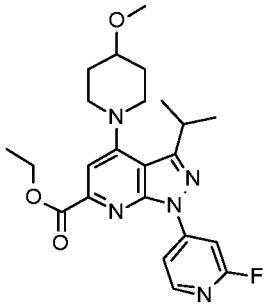
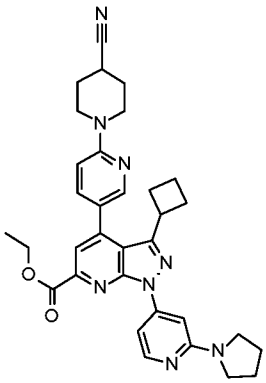
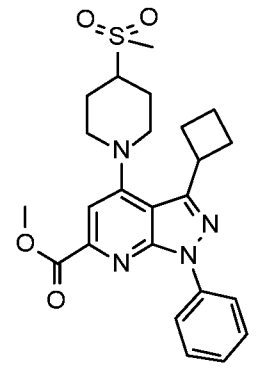
Int.	Structure	Name	SM	method	MW	Mes
E092		methyl 1-(4-fluorophenyl)-3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP05	I3, Specific example	440	441
E093		ethyl 4-[4-(4-cyano-1-piperidyl)phenyl]-3-isopropyl-1-(2-pyrrolidin-1-yl-4-pyridyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP12, AMP22	I1	563	564
E094		ethyl 3-isopropyl-4-[2-methoxyethyl(methyl)amino]-1-(*m*-tolyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP01	I1	410	411
E095		ethyl 3-isopropyl-1-(*m*-tolyl)-4-(8-oxa-2-azaspiro[4.5]decan-2-yl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP01	I3	462	463

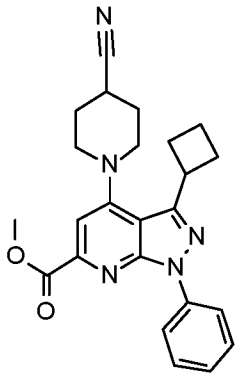
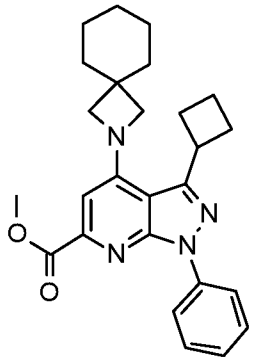
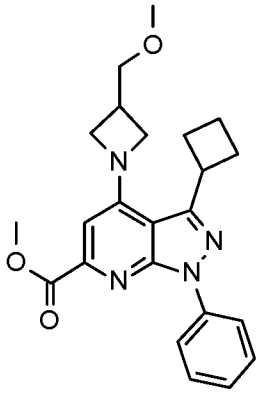
Int.	Structure	Name	SM	method	MW	Mes
E096		methyl 4-(4-butoxy-1-piperidyl)-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP05	I3	468	467
E097		methyl 1-(4-fluorophenyl)-3-isopropyl-4-(4-methoxy-4-methyl-1-piperidyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP05	I3	440	441
E098		methyl 1-(4-fluorophenyl)-4-(4-isobutoxy-1-piperidyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP05	I3	468	469

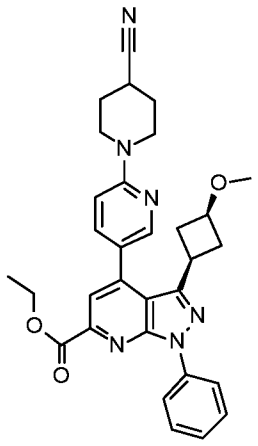
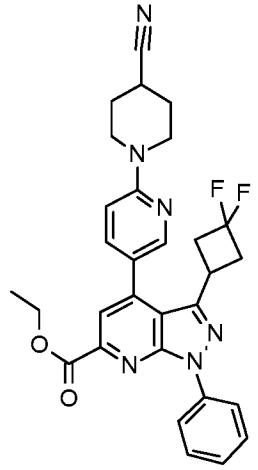
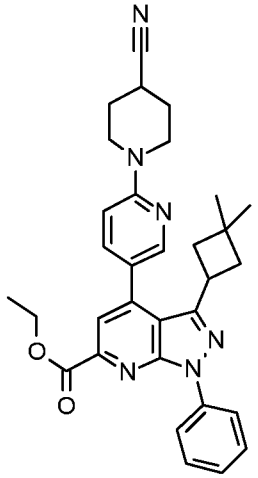
Int.	Structure	Name	SM	method	MW	Mes
E099		methyl 1-(4-fluorophenyl)-3-isopropyl-4-(1-oxa-7-azaspiro[3.5]nonan-7-yl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP05	I3	438	439
E100		methyl 4-[3-(difluoromethyl)-1-piperidyl]-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP05	I3	446	447
E101		methyl 1-(4-fluorophenyl)-3-isopropyl-4-(6-oxa-2-azaspiro[3.5]nonan-2-yl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP05	I3	438	439

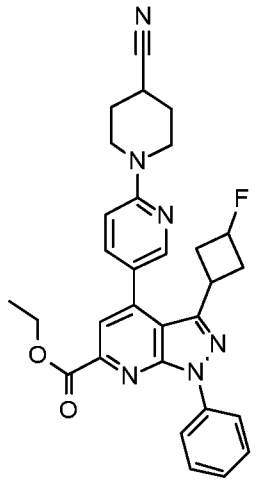
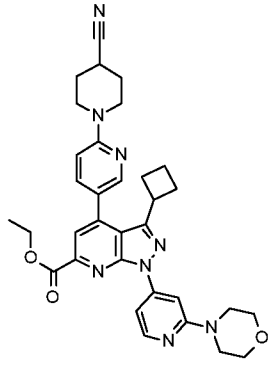
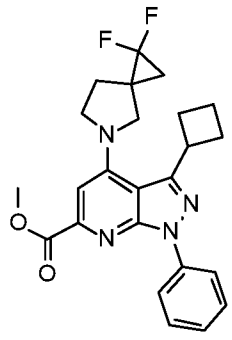
Int.	Structure	Name	SM	method	MW	Mes
E102		methyl 1-(4-fluorophenyl)-3-isopropyl-4-(1-oxa-8-azaspiro[4.5]decan-8-yl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP05	I3	452	453
E103		methyl 3-cyclobutyl-1-phenyl-4-(1-piperidyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	390	391
E104		methyl 3-cyclobutyl-4-[4-(2-methoxyethyl)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	448	449
E105		methyl 4-(2-azaspiro[3.4]octan-2-yl)-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	416	417

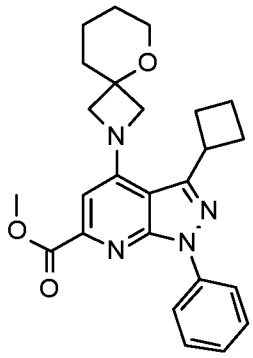
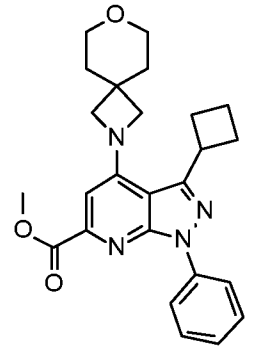
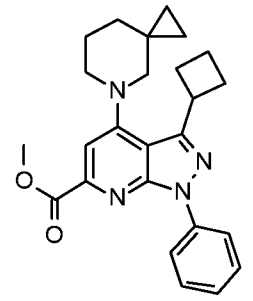
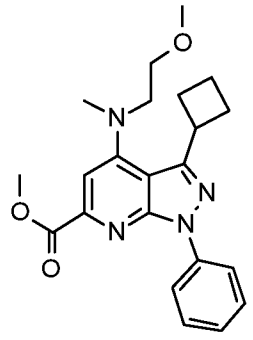
Int.	Structure	Name	SM	method	MW	Mes
E106		methyl 3-cyclobutyl-4-[4-(methoxymethyl)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	434	435
E107		methyl 4-(3-azabicyclo[3.1.0]hexan-3-yl)-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	388	389
E108		ethyl 1-(2-bromo-4-pyridyl)-3-isopropyl-4-(4-methoxy-1-piperidyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	E109	I4	501-503	502-504
E109		ethyl 3-isopropyl-4-(4-methoxy-1-piperidyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP08	I3	346	347

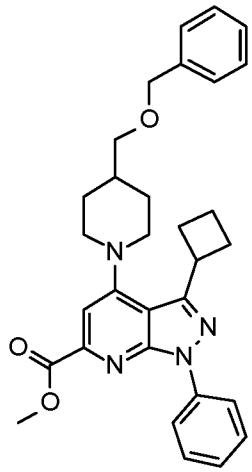
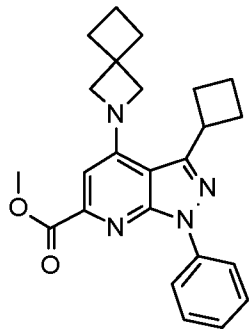
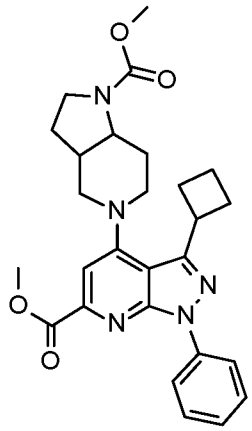
Int.	Structure	Name	SM	method	MW	Mes
E110		ethyl 3-isopropyl-4-(4-methoxy-1-piperidyl)-1-(2-pyrrolidin-1-yl-4-pyridyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	E111	I12, Specific example	492	493
E111		ethyl 1-(2-fluoro-4-pyridyl)-3-isopropyl-4-(4-methoxy-1-piperidyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	E109	I4, Specific example	441	442
E112		ethyl 4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-cyclobutyl-1-(2-pyrrolidin-1-yl-4-pyridyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP09, AMP34	I1	576	577
E113		methyl 3-cyclobutyl-4-(4-methylsulfonyl-1-piperidyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	468	469

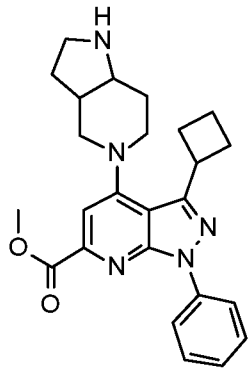
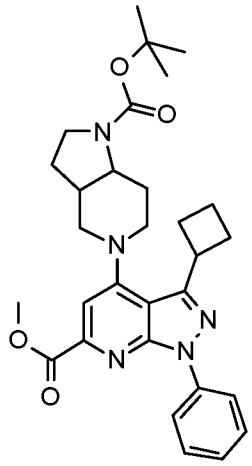
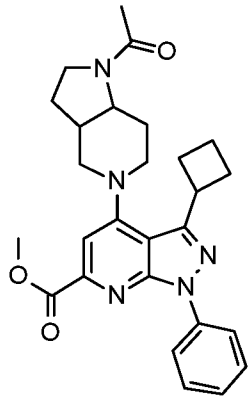
Int.	Structure	Name	SM	method	MW	Mes
E114		methyl 4-(4-cyano-1-piperidyl)-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	415	416
E115		methyl 4-(2-azaspiro[3.5]nonan-2-yl)-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	430	431
E116		methyl 3-cyclobutyl-4-[3-(methoxymethyl)azetidin-1-yl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	406	407

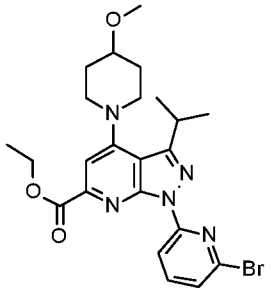
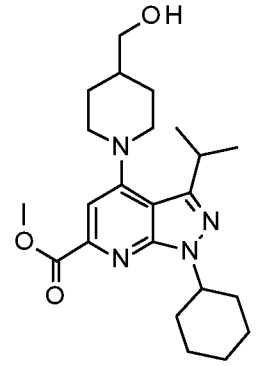
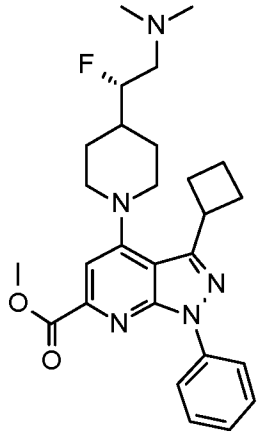
Int.	Structure	Name	SM	method	MW	Mes
E117		ethyl 4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-(3-methoxycyclobutyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP09, AMP42	I1	536	537
E118		ethyl 4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-(3,3-difluorocyclobutyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP09, AMP43	I1	542	543
E119		ethyl 4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-(3,3-dimethylcyclobutyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP09, AMP44	I1	534	535

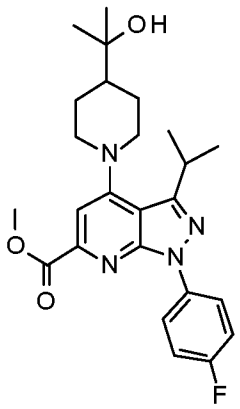
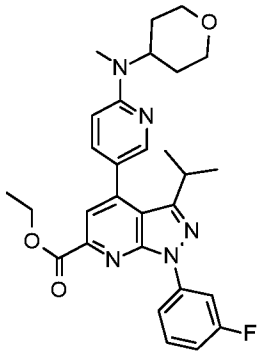
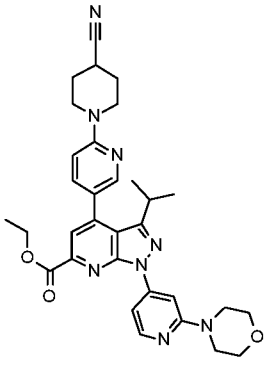
Int.	Structure	Name	SM	method	MW	Mes
E120		ethyl 4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-(3-fluorocyclobutyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP09, AMP45	I1	524	525
E121		ethyl 4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-cyclobutyl-1-(2-morpholino-4-pyridyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP09, AMP33	I1	592	593
E122		methyl 3-cyclobutyl-4-(2,2-difluoro-5-azaspiro[2.4]heptan-5-yl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	438	439

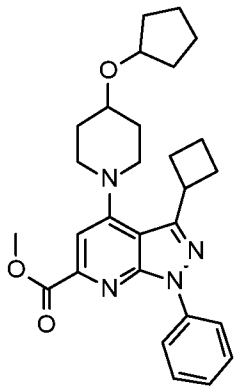
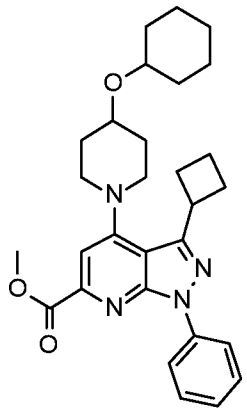
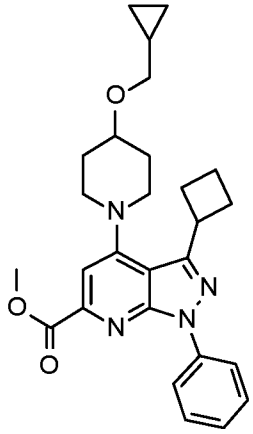
Int.	Structure	Name	SM	method	MW	Mes
E123		methyl 3-cyclobutyl-4-(5-oxa-2-azaspiro[3.5]nonan-2-yl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	432	433
E124		methyl 3-cyclobutyl-4-(7-oxa-2-azaspiro[3.5]nonan-2-yl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	432	433
E125		methyl 4-(5-azaspiro[2.5]octan-5-yl)-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	416	417
E126		methyl 3-cyclobutyl-4-[2-methoxyethyl(methyl)amino]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	394	395

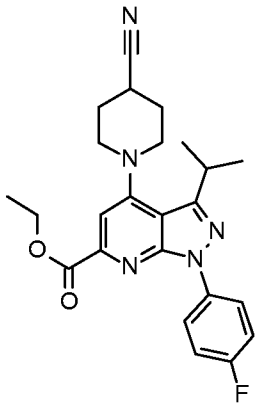
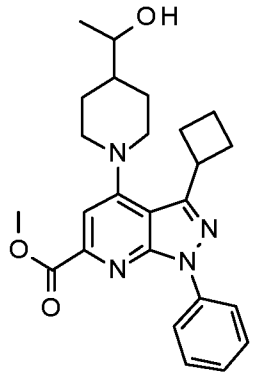
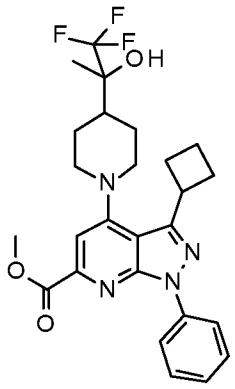
Int.	Structure	Name	SM	method	MW	Mes
E127		methyl 4-[4-(benzyloxymethyl)-1-piperidyl]-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	510	511
E128		methyl 4-(2-azaspiro[3.3]heptan-2-yl)-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	402	403
E129		methyl 3-cyclobutyl-4-(1-methoxycarbonyl-3,3a,4,6,7,7a-hexahydro-2*H*-pyrrolo[3,2-*c*]pyridin-5-yl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E130	I11, Specific example	489	490

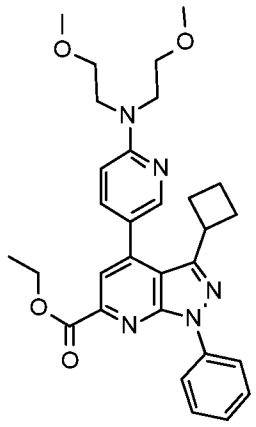
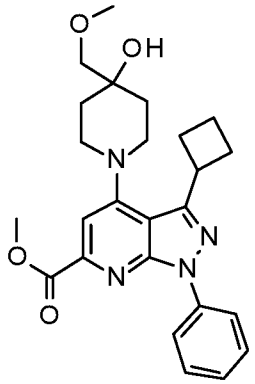
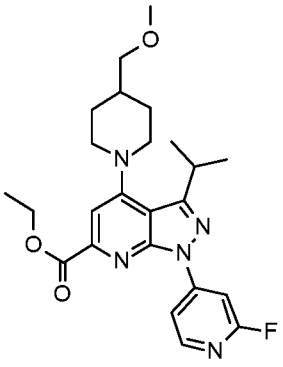
Int.	Structure	Name	SM	method	MW	Mes
E130		methyl 4-(1,2,3,3a,4,6,7,7a-octahydropyrrolo[3,2-*c*]pyridin-5-yl)-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E131	Specific example	431	432
E131		methyl 4-(1-*tert*-butoxycarbonyl-3,3a,4,6,7,7a-hexahydro-2*H*-pyrrolo[3,2-*c*]pyridin-5-yl)-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	531	532
E132		methyl 4-(1-acetyl-3,3a,4,6,7,7a-hexahydro-2*H*-pyrrolo[3,2-*c*]pyridin-5-yl)-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E130	I11, Specific example	473	474

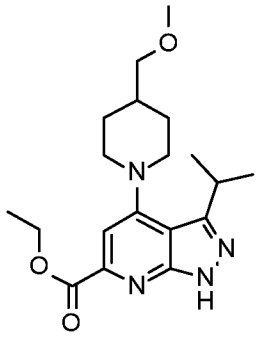
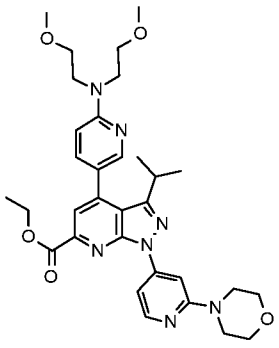
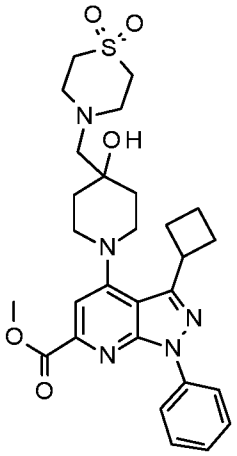
Int.	Structure	Name	SM	method	MW	Mes
E133		ethyl 1-(6-bromo-2-pyridyl)-3-isopropyl-4-(4-methoxy-1-piperidyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	E109	I5, Specific example	501-503	502-504
E134		methyl 1-cyclohexyl-4-[4-(hydroxymethyl)-1-piperidyl]-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP12	I3	414	415
E135		methyl 3-cyclobutyl-4-[4-[(1*S*)-2-(dimethylamino)-1-fluoro-ethyl]-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02, AMI03	I3	479	480

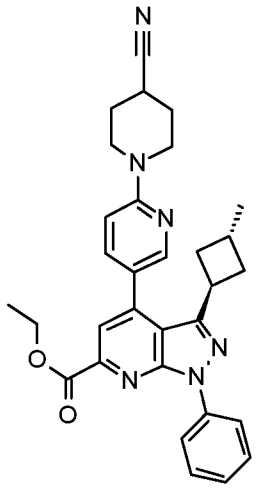
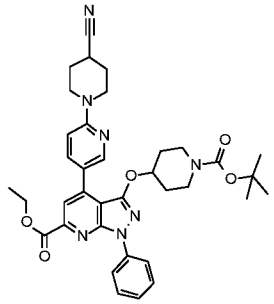
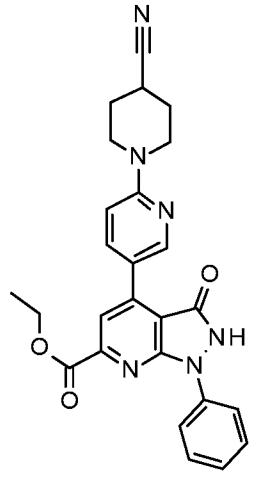
Int.	Structure	Name	SM	method	MW	Mes
E136		methyl 1-(4-fluorophenyl)-4-[4-(1-hydroxy-1-methyl-ethyl)-1-piperidyl]-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP05	I3	454	455
E137		ethyl 1-(3-fluorophenyl)-3-isopropyl-4-[6-[methyl(tetrahydropyran-4-yl)amino]-3-pyridyl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP10, AMP12	I1	517	518
E138		ethyl 4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-isopropyl-1-(2-morpholino-4-pyridyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP09, AMP21	I1	580	581

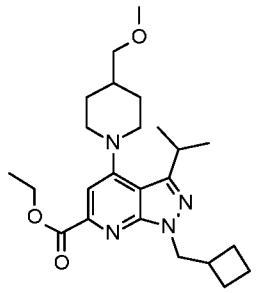
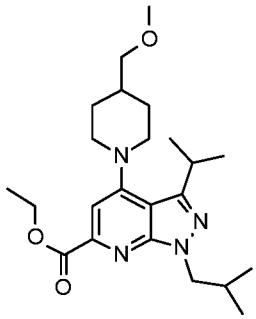
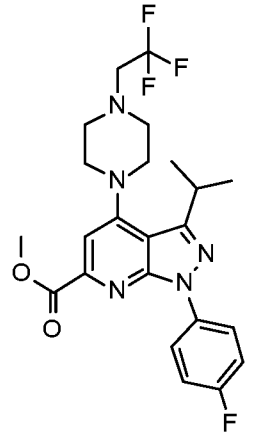
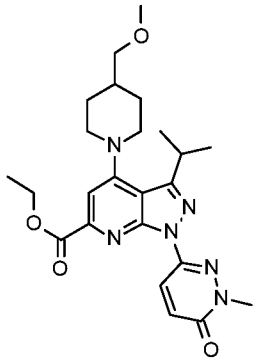
Int.	Structure	Name	SM	method	MW	Mes
E139		methyl 3-cyclobutyl-4-[4-(cyclopentoxy)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	474	475
E140		methyl 3-cyclobutyl-4-[4-(cyclohexoxy)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	488	489
E141		methyl 3-cyclobutyl-4-[4-(cyclopropylmethoxy)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	460	461

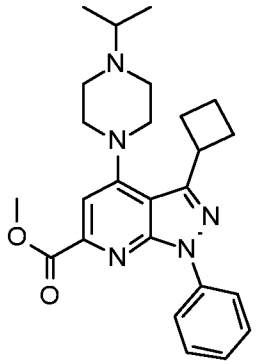
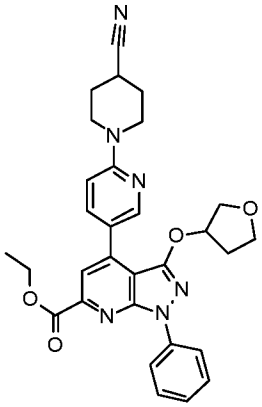
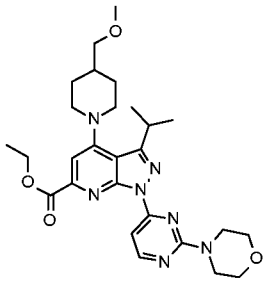
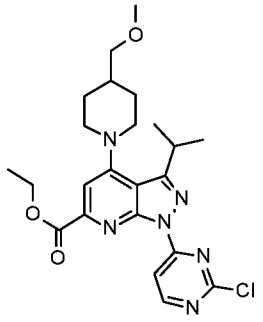
Int.	Structure	Name	SM	method	MW	Mes
E142		ethyl 4-(4-cyano-1-piperidyl)-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP09	I3	435	436
E143		methyl 3-cyclobutyl-4-[4-(1-hydroxyethyl)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	434	435
E144		methyl 3-cyclobutyl-1-phenyl-4-[4-(2,2,2-trifluoro-1-hydroxy-1-methyl-ethyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	502	503

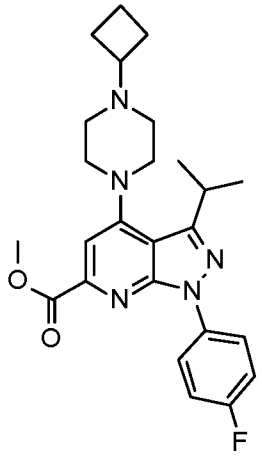
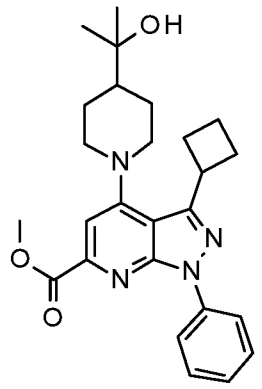
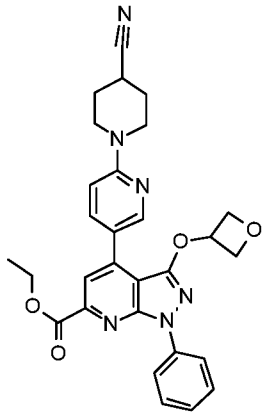
Int.	Structure	Name	SM	method	MW	Mes
E145		ethyl 4-[6-[bis(2-methoxyethyl)amino]-3-pyridyl]-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP23, AMP29	I1	529	530
E146		methyl 3-cyclobutyl-4-[4-hydroxy-4-(methoxymethyl)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02, AMI01	I3	450	451
E147		ethyl 1-(2-fluoro-4-pyridyl)-3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	E148	I4	455	456

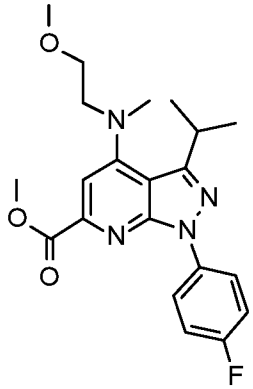
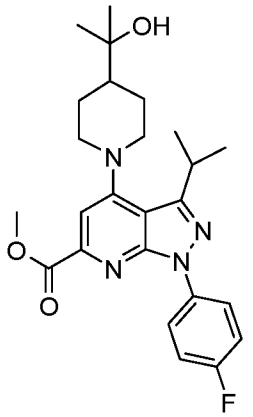
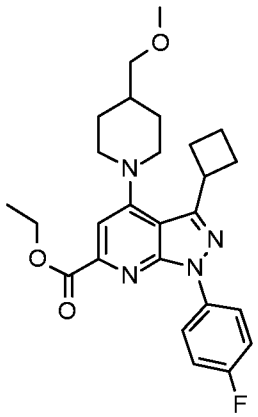
Int.	Structure	Name	SM	method	MW	Mes
E148		ethyl 3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP08	I3	360	361
E149		ethyl 4-[6-[bis(2-methoxyethyl)amino]-3-pyridyl]-3-isopropyl-1-(2-morpholino-4-pyridyl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP23, AMP21	I1	603	604
E150		methyl 3-cyclobutyl-4-[4-[(1,1-dioxo-1,4-thiazinan-4-yl)methyl]-4-hydroxy-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02, AMI02	I3	553	554

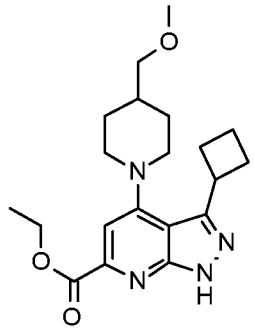
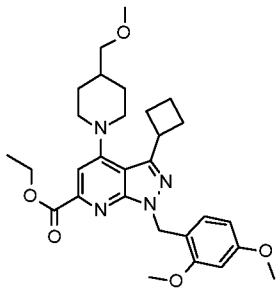
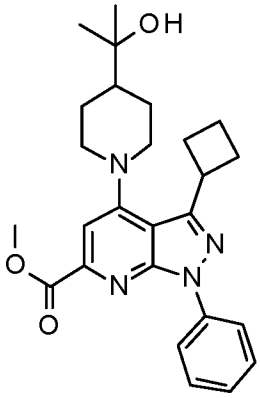
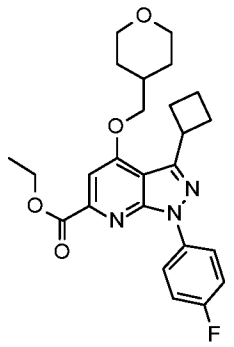
Int.	Structure	Name	SM	method	MW	Mes
E151		ethyl 4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-(3-methylcyclobutyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP09, AMP46	I1	520	521
E152		ethyl 3-[(1-*tert*-butoxycarbonyl-4-piperidyl)oxy]-4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E153	I13, Specific example	651	
E153		ethyl 4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-oxo-1-phenyl-2*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP09, 70373-98-7	I1	468	469

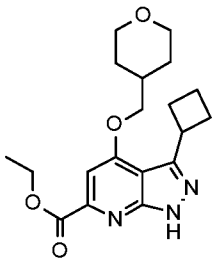
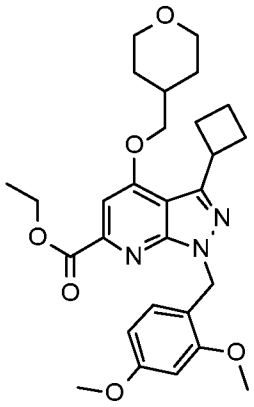
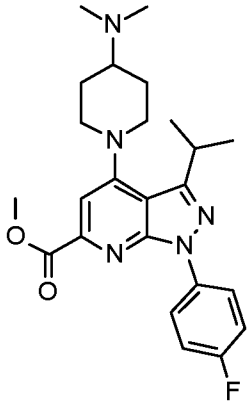
Int.	Structure	Name	SM	method	MW	Mes
E154		ethyl 1-(cyclobutylmethyl)-3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	E148	I6, Specific example	428	429
E155		ethyl 1-isobutyl-3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	E148	I6	416	417
E156		methyl 1-(4-fluorophenyl)-3-isopropyl-4-[4-(2,2,2-trifluoroethyl)piperazin-1-yl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP05	I3	479	480
E157		ethyl 3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]-1-(1-methyl-6-oxo-pyridazin-3-yl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	E148	I7	468	469

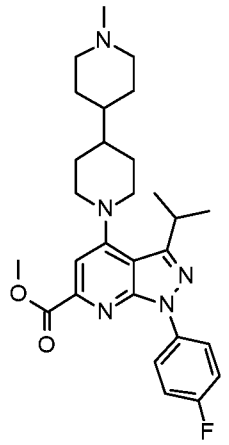
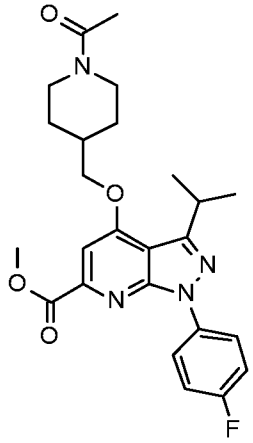
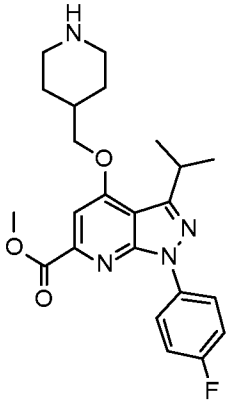
Int.	Structure	Name	SM	method	MW	Mes
E158		methyl 3-cyclobutyl-4-(4-isopropylpiperazin-1-yl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	433	434
E159		ethyl 4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-1-phenyl-3-tetrahydrofuran-3-yloxy-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E153	I13	538	539
E160		ethyl 3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]-1-(2-morpholinopyrimidin-4-yl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	E161	I12	523	524
E161		ethyl 1-(2-chloropyrimidin-4-yl)-3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	E148	I5	472-474	473-475

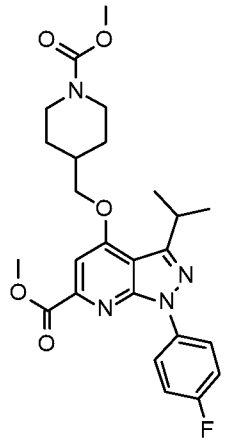
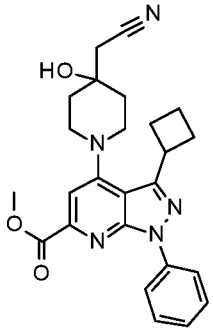
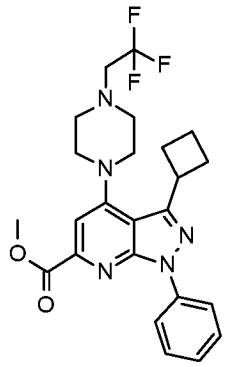
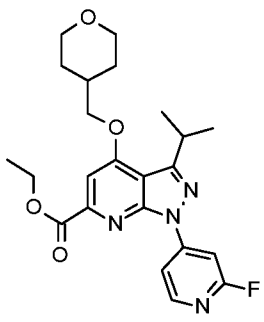
Int.	Structure	Name	SM	method	MW	Mes
E162		methyl 4-(4-cyclobutylpiperazin-1-yl)-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP05	I3	451	452
E163		methyl 3-cyclobutyl-4-[4-(1-hydroxy-1-methyl-ethyl)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	448	449
E164		ethyl 4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-(oxetan-3-yloxy)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E153	I13	524	525

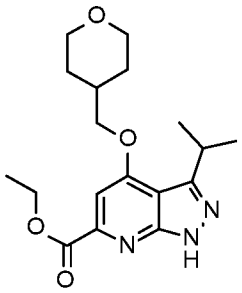
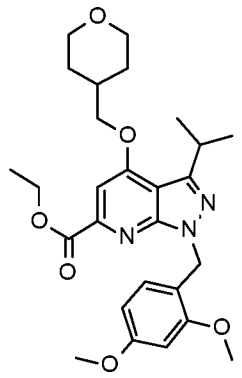
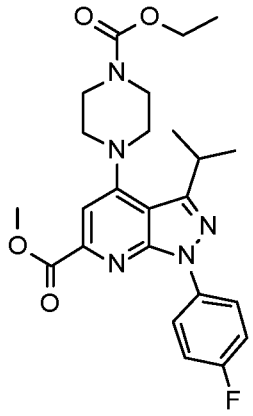
Int.	Structure	Name	SM	method	MW	Mes
E165		methyl 1-(4-fluorophenyl)-3-isopropyl-4-[2-methoxyethyl(methyl) amino]pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP05	I3	400	401
E166		methyl 1-(4-fluorophenyl)-4-[4-(1-hydroxy-1-methyl-ethyl)-1-piperidyl]-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP05	I3	454	455
E167		ethyl 3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(methoxymethyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	E168	I4	466	467

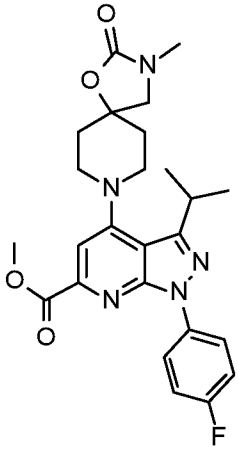
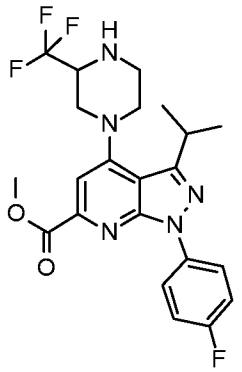
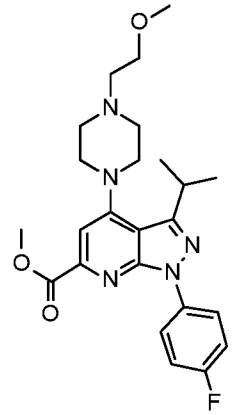
Int.	Structure	Name	SM	method	MW	Mes
E168		ethyl 3-cyclobutyl-4-[4-(methoxymethyl)-1-piperidyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E169	I15	372	373
E169		ethyl 3-cyclobutyl-1-[(2,4-dimethoxyphenyl)methyl]-4-[4-(methoxymethyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP14	I3	522	523
E170		methyl 3-cyclobutyl-4-[4-(1-hydroxy-1-methyl-ethyl)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	448	449
E171		ethyl 3-cyclobutyl-1-(4-fluorophenyl)-4-(tetrahydropyran-4-ylmethoxy)pyrazolo[3,4-*b*]pyridine-6-carboxylate	E172	I16, Specific example	453	454

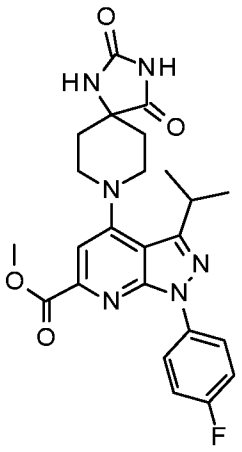
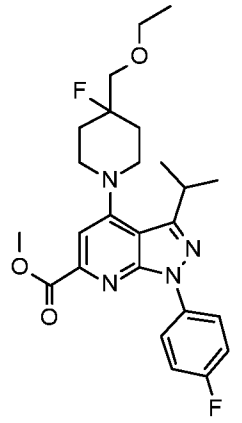
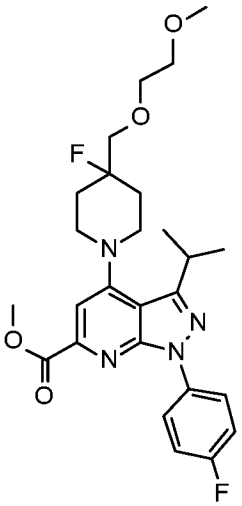
Int.	Structure	Name	SM	method	MW	Mes
E172		ethyl 3-cyclobutyl-4-(tetrahydropyran-4-ylmethoxy)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E173	I15	359	360
E173		ethyl 3-cyclobutyl-1-[(2,4-dimethoxyphenyl)methyl]-4-(tetrahydropyran-4-ylmethoxy)pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP15	I14	509	510
E174		methyl 4-[4-(dimethylamino)-1-piperidyl]-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP05	I3	439	440

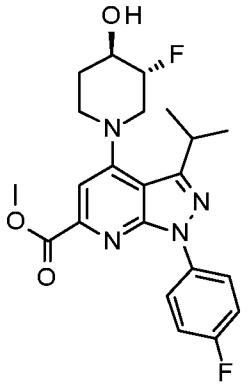
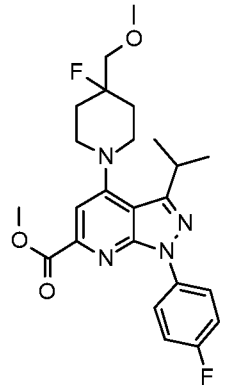
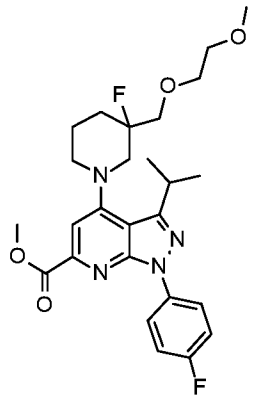
Int.	Structure	Name	SM	method	MW	Mes
E175		methyl 1-(4-fluorophenyl)-3-isopropyl-4-[4-(1-methyl-4-piperidyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP05	I3	493	494
E176		methyl 4-[(1-acetyl-4-piperidyl)methoxy]-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E177	I11, Specific example	468	469
E177		methyl 1-(4-fluorophenyl)-3-isopropyl-4-(4-piperidylmethoxy)pyrazolo[3,4-*b*]pyridine-6-carboxylate	A263	I9	426	427

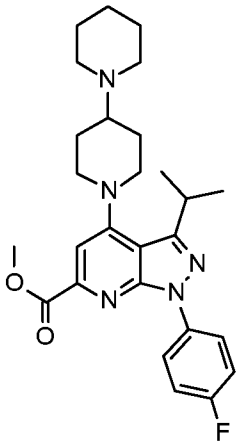
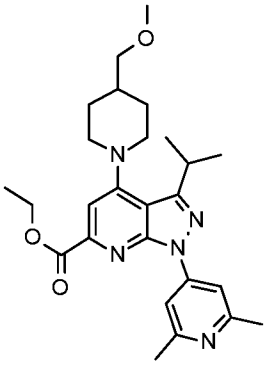
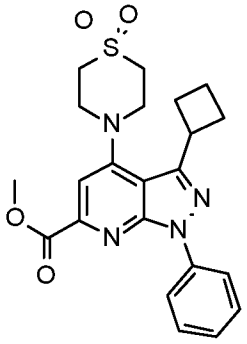
Int.	Structure	Name	SM	method	MW	Mes
E178		methyl 1-(4-fluorophenyl)-3-isopropyl-4-[(1-methoxycarbonyl-4-piperidyl)methoxy]pyrazolo[3,4-*b*]pyridine-6-carboxylate	E177	I11, Specific example	484	485
E179		methyl 4-[4-(cyanomethyl)-4-hydroxy-1-piperidyl]-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02, AMI09	I3	445	446
E180		methyl 3-cyclobutyl-1-phenyl-4-[4-(2,2,2-trifluoroethyl)piperazin-1-yl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	473	474
E181		ethyl 1-(2-fluoro-4-pyridyl)-3-isopropyl-4-(tetrahydropyran-4-ylmethoxy)pyrazolo[3,4-*b*]pyridine-6-carboxylate	E182	I4	442	443

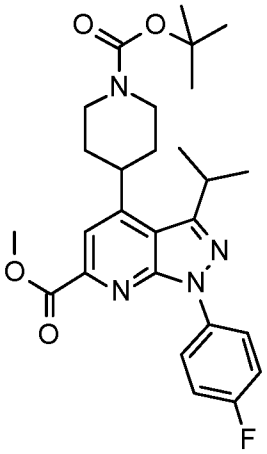
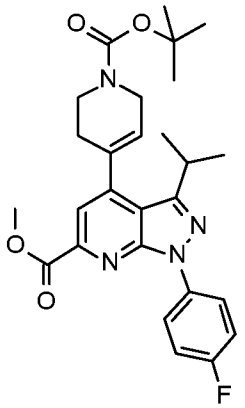
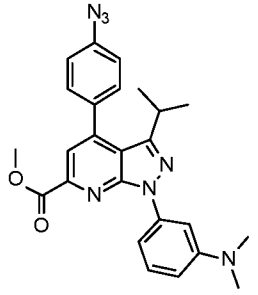
Int.	Structure	Name	SM	method	MW	Mes
E182		ethyl 3-isopropyl-4-(tetrahydropyran-4-ylmethoxy)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E183	I15	347	348
E183		ethyl 1-[(2,4-dimethoxyphenyl)methyl]-3-isopropyl-4-(tetrahydropyran-4-ylmethoxy)pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP06	I14, Specific example	497	498
E184		methyl 4-(4-ethoxycarbonylpiperazin-1-yl)-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP05	I3	469	470

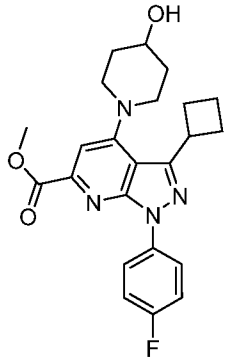
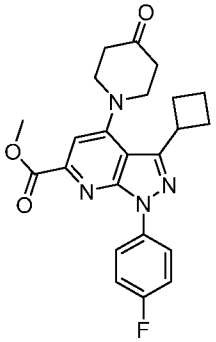
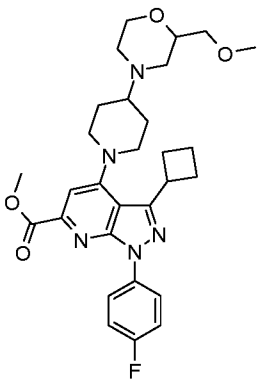
Int.	Structure	Name	SM	method	MW	Mes
E185		methyl 1-(4-fluorophenyl)-3-isopropyl-4-(3-methyl-2-oxo-1-oxa-3,8-diazaspiro[4.5]decan-8-yl)pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP05	I3	481	482
E186		methyl 1-(4-fluorophenyl)-3-isopropyl-4-[3-(trifluoromethyl)piperazin-1-yl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP05	I3	465	466
E187		methyl 1-(4-fluorophenyl)-3-isopropyl-4-[4-(2-methoxyethyl)piperazin-1-yl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP05	I3	455	456

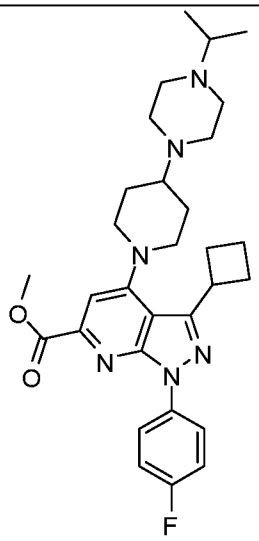
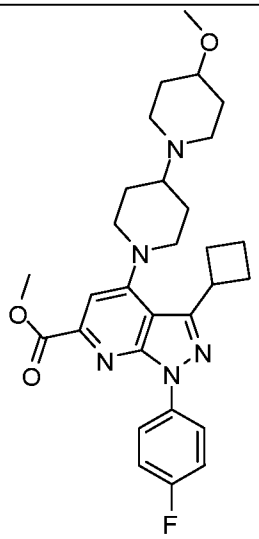
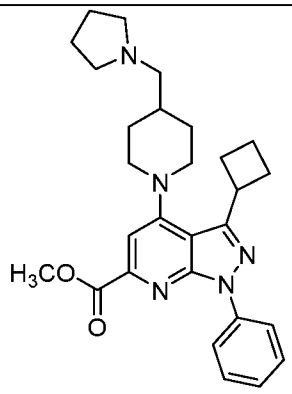
Int.	Structure	Name	SM	method	MW	Mes
E188		methyl 4-(2,4-dioxo-1,3,8-triazaspiro[4.5]decan-8-yl)-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP05	I3	480	481
E189		methyl 4-[4-(ethoxymethyl)-4-fluoro-1-piperidyl]-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP05, AMI04	I3	472	473
E190		methyl 4-[4-fluoro-4-(2-methoxyethoxymethyl)-1-piperidyl]-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP05, AMI05	I3	502	503

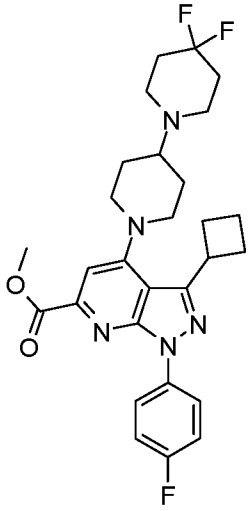
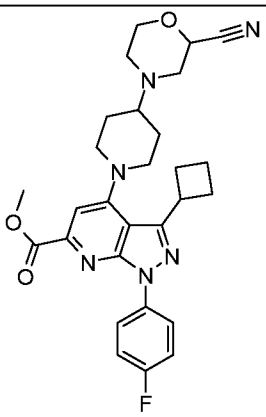
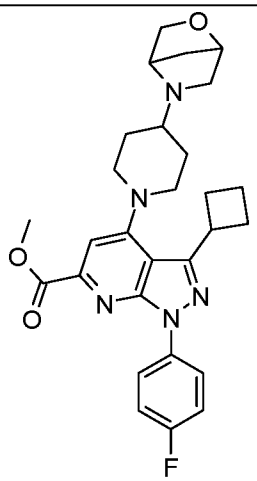
Int.	Structure	Name	SM	method	MW	Mes
E191		methyl 4-[(3*R*,4*R*)-3-fluoro-4-hydroxy-1-piperidyl]-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP05, AMI06	I3	430	431
E192		methyl 4-[4-fluoro-4-(methoxymethyl)-1-piperidyl]-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP05, AMI07	I3	458	459
E193		methyl 4-[3-fluoro-3-(2-methoxyethoxymethyl)-1-piperidyl]-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP05, AMI08	I3	502	503

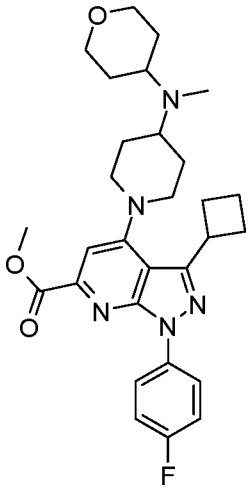
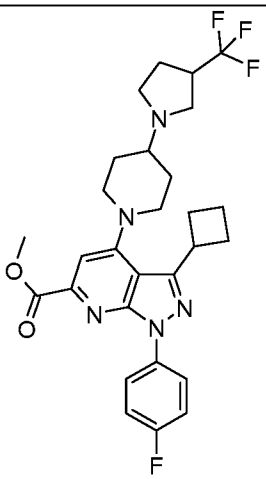
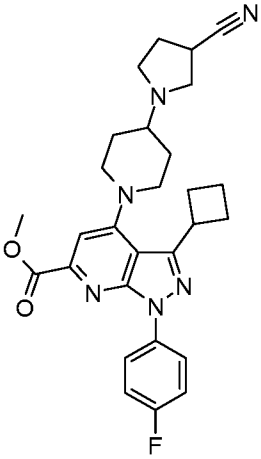
Int.	Structure	Name	SM	method	MW	Mes
E194		methyl 1-(4-fluorophenyl)-3-isopropyl-4-[4-(1-piperidyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP05	I3	479	480
E195		ethyl 1-(2,6-dimethyl-4-pyridyl)-3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	E148	I4	465	466
E196		methyl 3-cyclobutyl-4-(1,1-dioxo-1,4-thiazinan-4-yl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	440	441

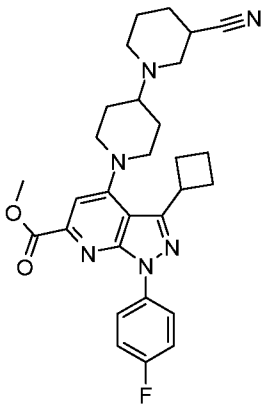
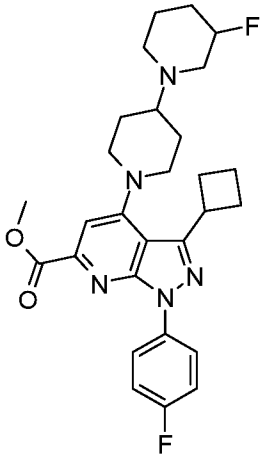
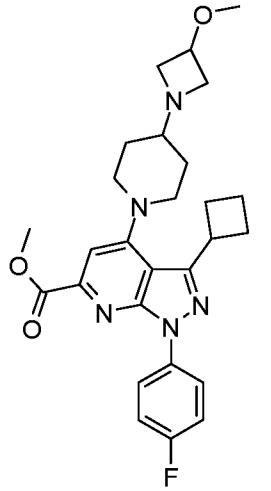
Int.	Structure	Name	SM	method	MW	Mes
E197		methyl 4-(1-*tert*-butoxycarbonyl-4-piperidyl)-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E198	Specific example	496	497
E198		methyl 4-(1-*tert*-butoxycarbonyl-3,6-dihydro-2*H*-pyridin-4-yl)-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP05	I2, Specific example	494	495
E199		methyl 4-(4-azidophenyl)-1-[3-(dimethylamino)phenyl]-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E074	Specific example	455	456

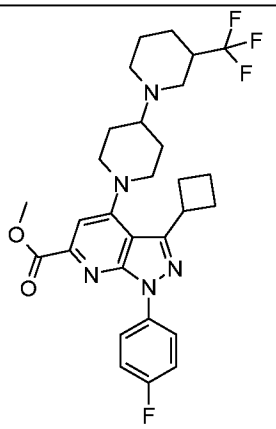
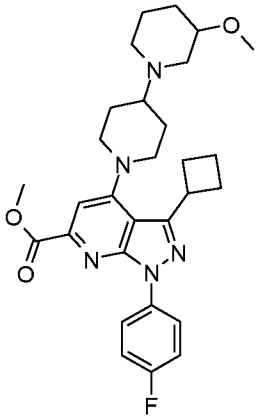
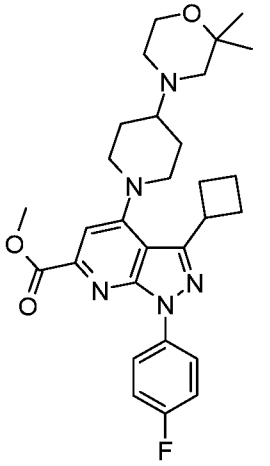
Int.	Structure	Name	SM	method	MW	Mes
E352		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-(4-hydroxypiperidin-1-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP19	I3	424	425
E353		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-(4-oxopiperidin-1-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E352	Specific example	422	423
E354		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[2-(methoxymethyl)morpholin-4-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E353	Specific example	537	538

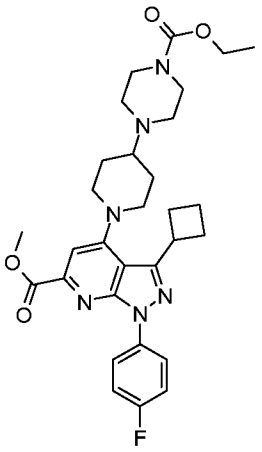
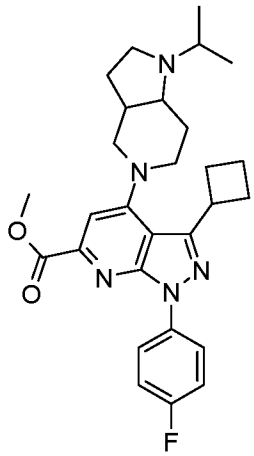
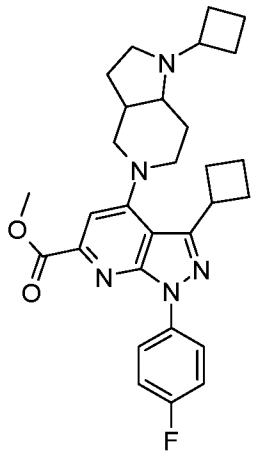
Int.	Structure	Name	SM	method	MW	Mes
E355		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(4-isopropylpiperazin-1-yl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP19, 202991-78-4	I3	534	535
E356		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(4-methoxy-1-piperidyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP19, AMI10	I3, Specific example	522	523
E357		methyl 3-cyclobutyl-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02, 683772-11-4	I3, Specific example	473	474

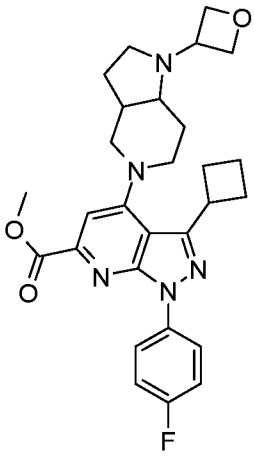
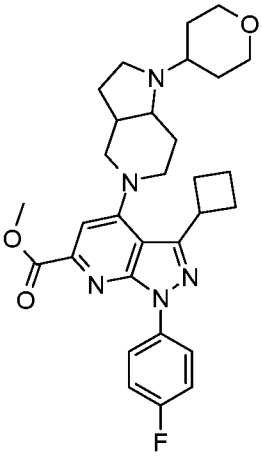
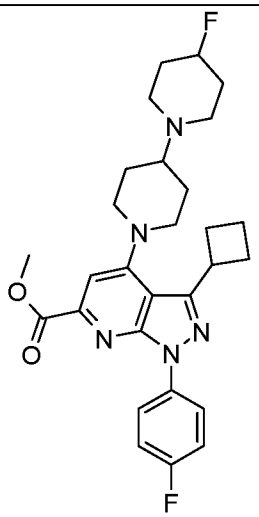
Int.	Structure	Name	SM	method	MW	Mes
E358		methyl 3-cyclobutyl-4-(4,4-difluoro[1,4'-bipiperidin]-1'-yl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E353	I18	527	528
E359		methyl 4-[4-(2-cyanomorpholin-4-yl)piperidin-1-yl]-3-cyclobutyl-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E353	I18	518	519
E360		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E353	I18	505	506

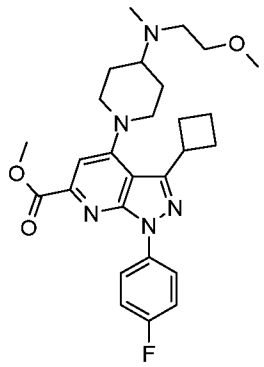
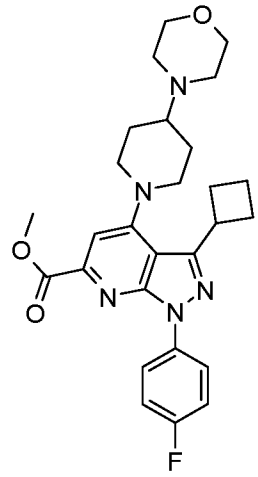
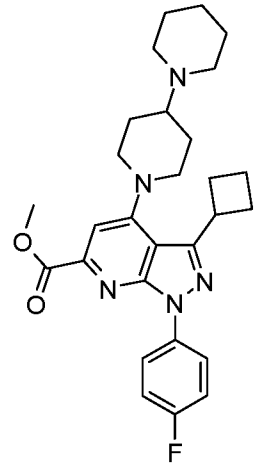
Int.	Structure	Name	SM	method	MW	Mes
E361		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[methyl(oxan-4-yl)amino]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E353	I18	521	522
E362		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[3-(trifluoromethyl)pyrrolidin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E353	I18	545	546
E363		methyl 4-[4-(3-cyanopyrrolidin-1-yl)piperidin-1-yl]-3-cyclobutyl-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E353	I18	502	503

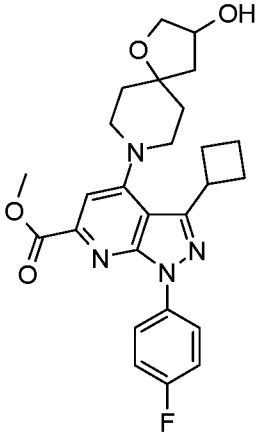
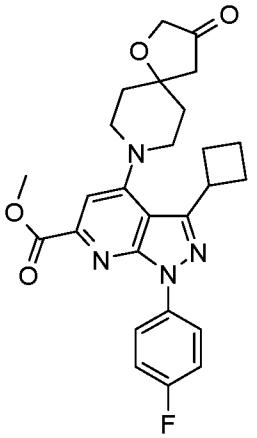
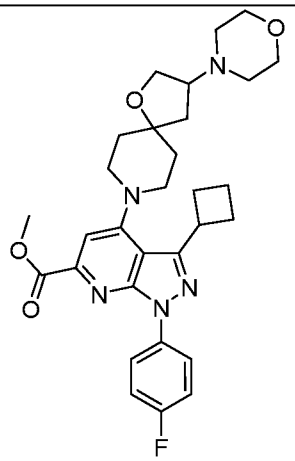
Int.	Structure	Name	SM	method	MW	Mes
E364		methyl 4-(3-cyano[1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E353	I18	516	517
E365		methyl 3-cyclobutyl-4-(3-fluoro[1,4'-bipiperidin]-1'-yl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E353	I18	509	510
E366		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(3-methoxyazetidin-1-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E353	I18	493	494

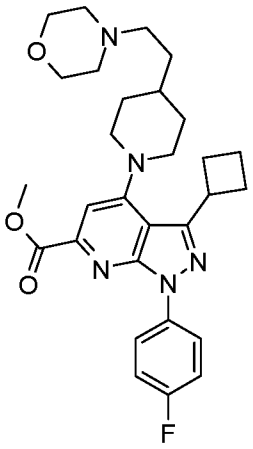
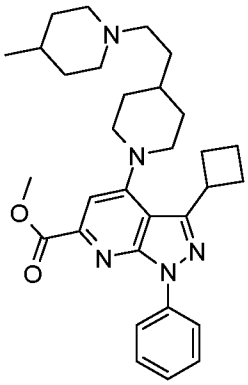
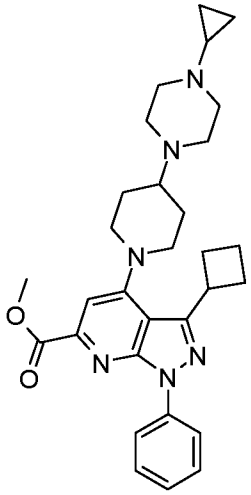
Int.	Structure	Name	SM	method	MW	Mes
E367		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-[3-(trifluoromethyl)[1,4'-bipiperidin]-1'-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E353	I18	559	560
E368		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-(3-methoxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E353	I18	521	522
E369		methyl 3-cyclobutyl-4-[4-(2,2-dimethylmorpholin-4-yl)piperidin-1-yl]-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E353	I18	521	522

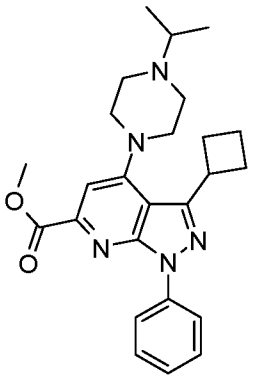
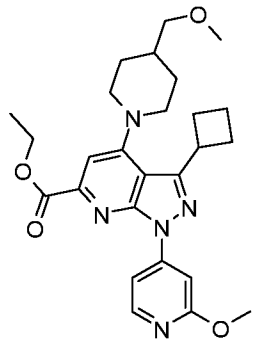
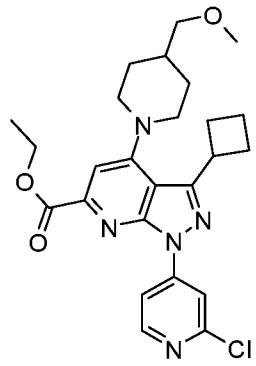
Int.	Structure	Name	SM	method	MW	Mes
E370		methyl 3-cyclobutyl-4-{4-[4-(ethoxycarbonyl)piperazin-1-yl]piperidin-1-yl}-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E353	I18	564	565
E371		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-[1-(propan-2-yl)octahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E514	I33	491	492
E372		methyl 3-cyclobutyl-4-(1-cyclobutyloctahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E514	I33	503	504

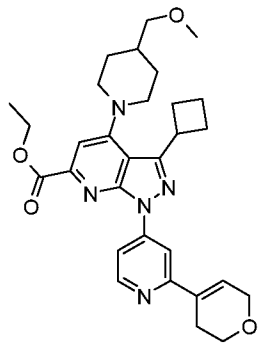
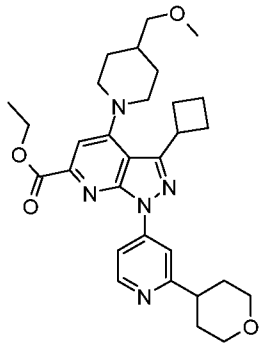
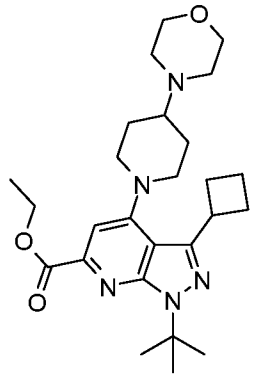
Int.	Structure	Name	SM	method	MW	Mes
E373		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-[1-(oxetan-3-yl)octahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E514	I33	505	506
E374		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-[1-(oxan-4-yl)octahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E514	I33	533	534
E375		methyl 3-cyclobutyl-4-(4-fluoro[1,4'-bipiperidin]-1'-yl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E353	I18	509	510

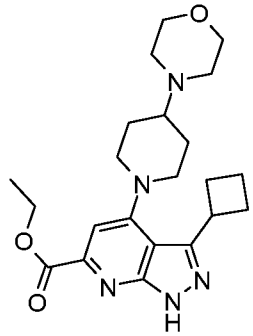
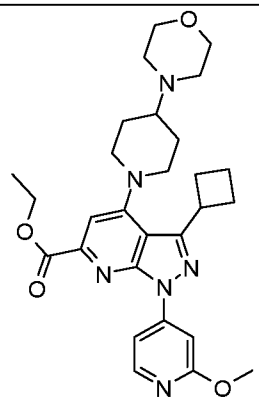
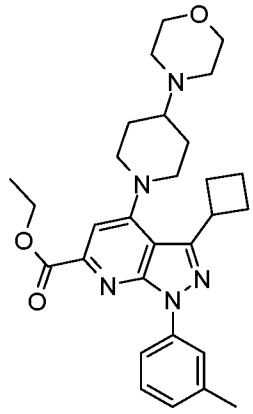
Int.	Structure	Name	SM	method	MW	Mes
E376		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[(2-methoxyethyl)(methyl)amino]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E353	I18	495	496
E377		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP19	I3	493	494
E378		methyl 4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP19	I3	491	492

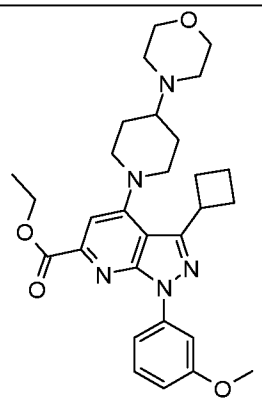
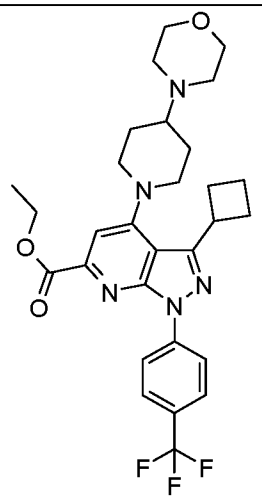
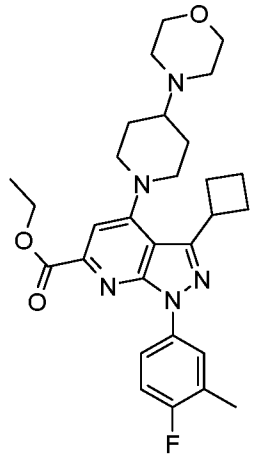
Int.	Structure	Name	SM	method	MW	Mes
E379		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-(3-hydroxy-1-oxa-8-azaspiro[4.5]decan-8-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP19	I3	480	481
E380		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-(3-oxo-1-oxa-8-azaspiro[4.5]decan-8-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E379	I23	478	479
E381		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-[3-(morpholin-4-yl)-1-oxa-8-azaspiro[4.5]decan-8-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E380	I18	533	534

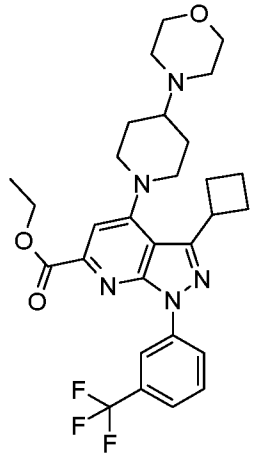
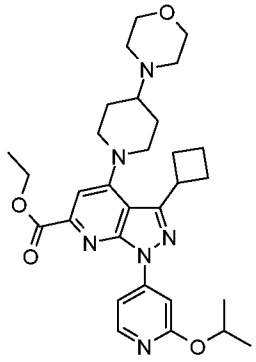
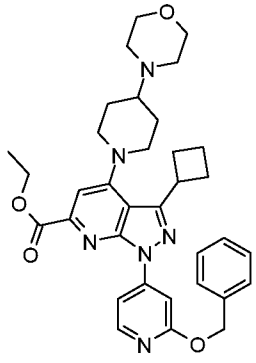
Int.	Structure	Name	SM	method	MW	Mes
E382		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[2-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP19	I3	521	522
E383		methyl 3-cyclobutyl-4-{4-[2-(4-methylpiperidin-1-yl)ethyl]piperidin-1-yl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	515	516
E384		methyl 3-cyclobutyl-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	514	515

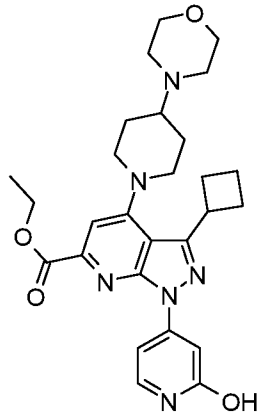
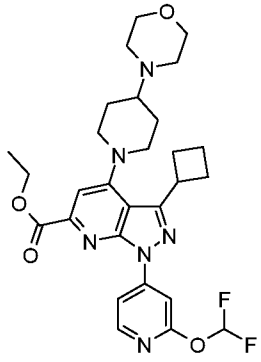
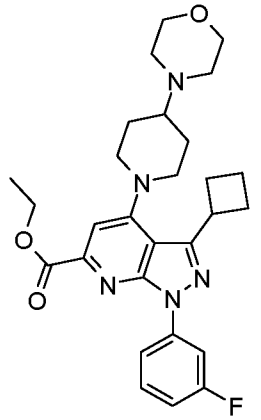
Int.	Structure	Name	SM	method	MW	Mes
E385		methyl 3-cyclobutyl-1-phenyl-4-[4-(propan-2-yl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	433	434
E388		ethyl 3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-(2-methoxypyridin-4-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E168	I4	479	480
E389		ethyl 1-(2-chloropyridin-4-yl)-3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E168	I4	484-486	485-487

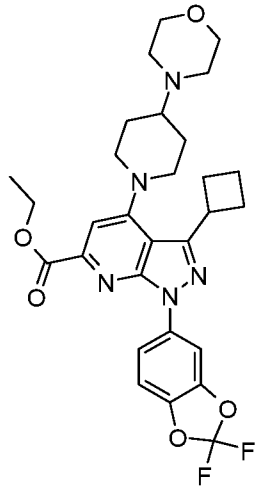
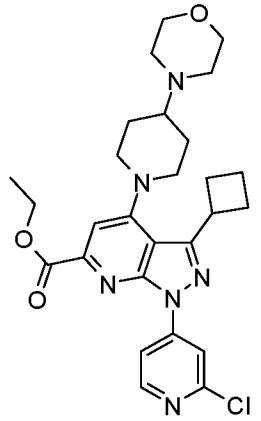
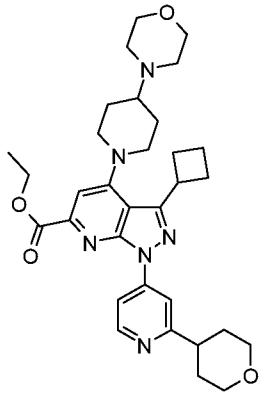
Int.	Structure	Name	SM	method	MW	Mes
E390		ethyl 3-cyclobutyl-1-[2-(3,6-dihydro-2*H*-pyran-4-yl)pyridin-4-yl]-4-[4-(methoxymethyl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E389	Specific example	531	532
E391		ethyl 3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-[2-(oxan-4-yl)pyridin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E390	Specific example	533	534
E392		ethyl 1-*tert*-butyl-3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP20	I3	469	470

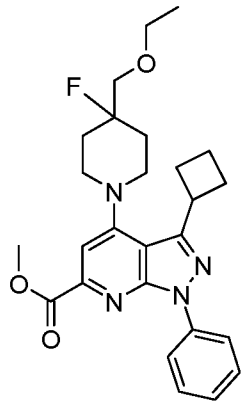
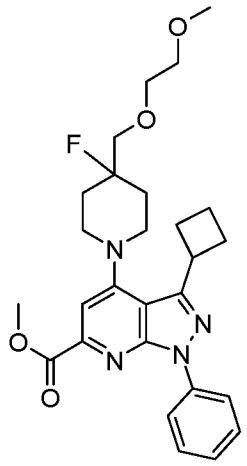
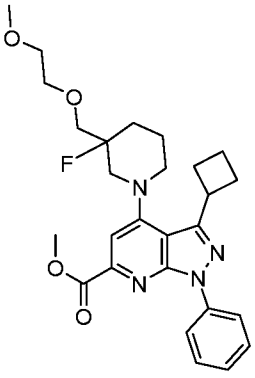
Int.	Structure	Name	SM	method	MW	Mes
E393		ethyl 3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E392	Specific example	413	414
E394		ethyl 3-cyclobutyl-1-(2-methoxypyridin-4-yl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E393	I4	520	521
E395		ethyl 3-cyclobutyl-1-(3-methylphenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E393	I4	503	504

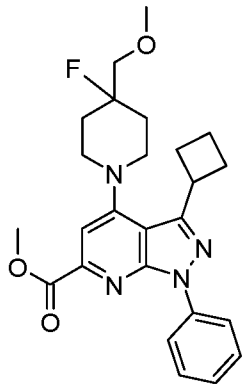
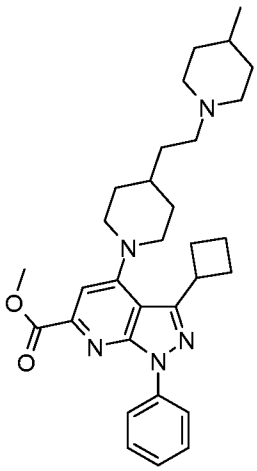
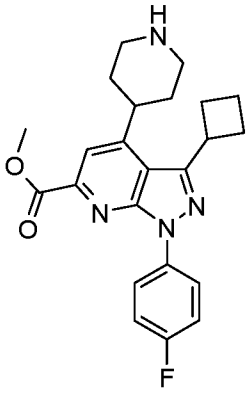
Int.	Structure	Name	SM	method	MW	Mes
E396		ethyl 3-cyclobutyl-1-(3-methoxyphenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E393	I4	519	520
E397		ethyl 3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-[4-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E393	I4	557	558
E398		ethyl 3-cyclobutyl-1-(4-fluoro-3-methylphenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E393	I4	521	522

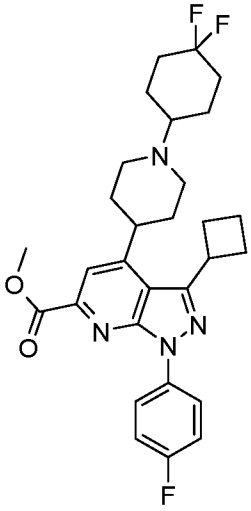
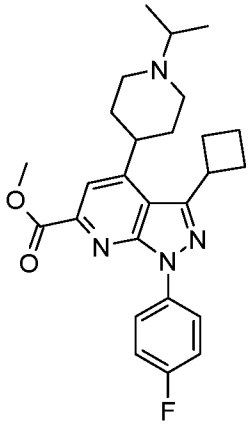
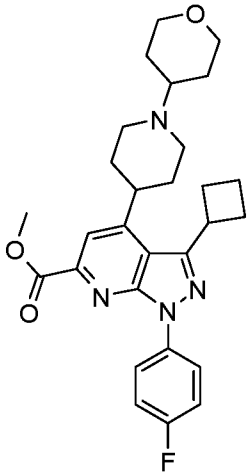
Int.	Structure	Name	SM	method	MW	Mes
E399		ethyl 3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E393	I4	557	558
E400		ethyl 3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-{2-[(propan-2-yl)oxy]pyridin-4-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E393	I4	548	549
E401		ethyl 1-[2-(benzyloxy)pyridin-4-yl]-3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E393	I4	596	597

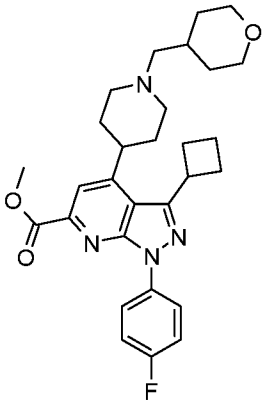
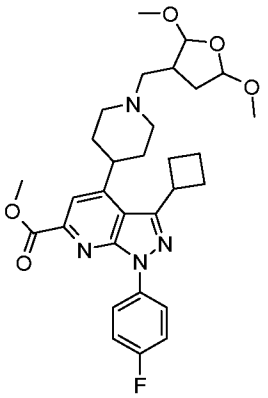
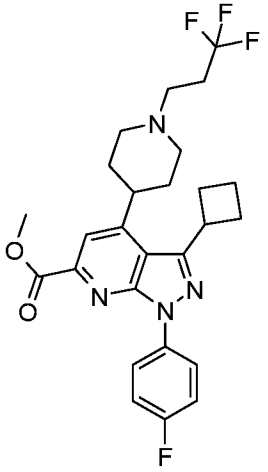
Int.	Structure	Name	SM	method	MW	Mes
E402		ethyl 3-cyclobutyl-1-(2-hydroxypyridin-4-yl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E401	Specific example	506	507
E403		ethyl 3-cyclobutyl-1-[2-(difluoromethoxy)pyridin-4-yl]-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E393	I4	556	557
E404		ethyl 3-cyclobutyl-1-(3-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E393	I4	507	508

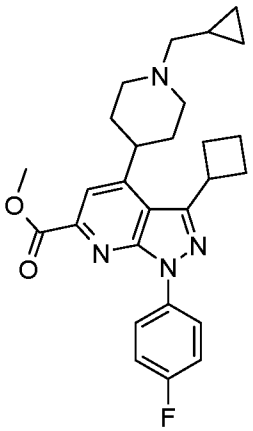
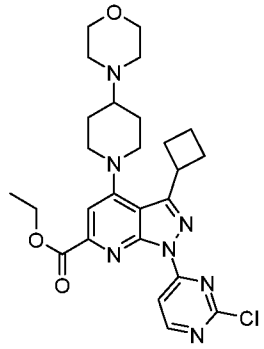
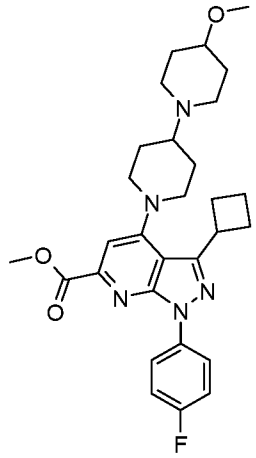
Int.	Structure	Name	SM	method	MW	Mes
E405		ethyl 3-cyclobutyl-1-(2,2-difluoro-2*H*-1,3-benzodioxol-5-yl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E393	I4	569	570
E406		ethyl 1-(2-chloropyridin-4-yl)-3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E393	I4	525-527	526-528
E407		ethyl 3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-[2-(oxan-4-yl)pyridin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E406	Specific example	574	575

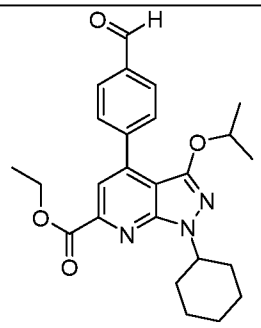
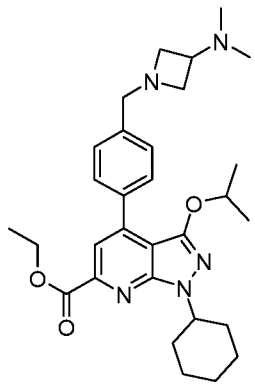
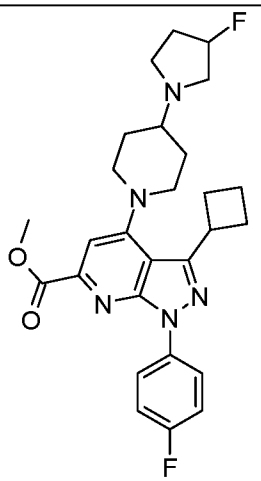
Int.	Structure	Name	SM	method	MW	Mes
E408		methyl 3-cyclobutyl-4-[4-(ethoxymethyl)-4-fluoropiperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02, AMI04	I3	466	467
E409		methyl 3-cyclobutyl-4-{4-fluoro-4-[(2-methoxyethoxy)methyl]piperidin-1-yl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02, AMI05	I3	496	497
E410		methyl 3-cyclobutyl-4-{3-fluoro-3-[(2-methoxyethoxy)methyl]piperidin-1-yl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02, AMI08	I3	496	497

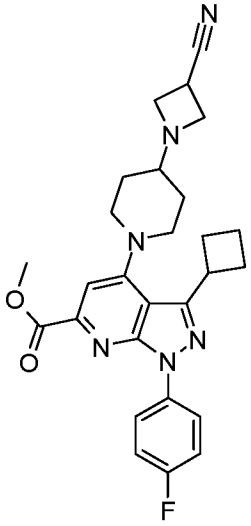
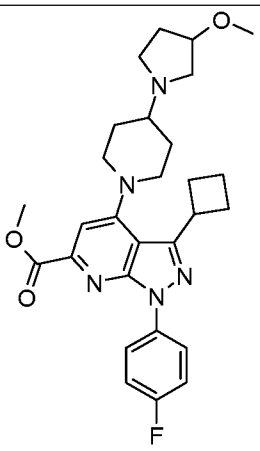
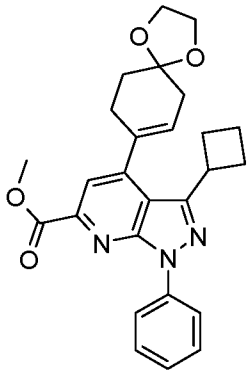
Int.	Structure	Name	SM	method	MW	Mes
E411		methyl 3-cyclobutyl-4-[4-fluoro-4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02, AMI07	I3	452	453
E412		methyl 3-cyclobutyl-4-{4-[2-(4-methylpiperidin-1-yl)ethyl]piperidin-1-yl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	I3	515	516
E413		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-(piperidin-4-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP19	Specific example	408	409

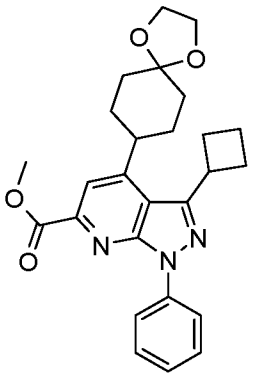
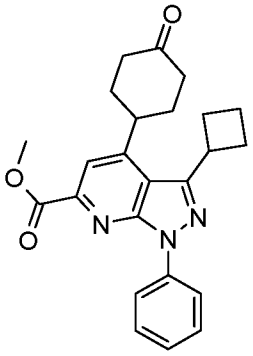
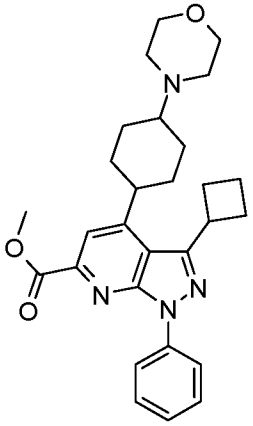
Int.	Structure	Name	SM	method	MW	Mes
E414		methyl 3-cyclobutyl-4-[1-(4,4-difluorocyclohexyl)piperidin-4-yl]-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E413	I18	526	527
E415		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-[1-(propan-2-yl)piperidin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E413	I18	450	451
E416		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-[1-(oxan-4-yl)piperidin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E413	I18	492	493

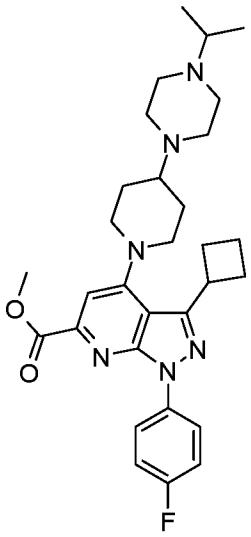
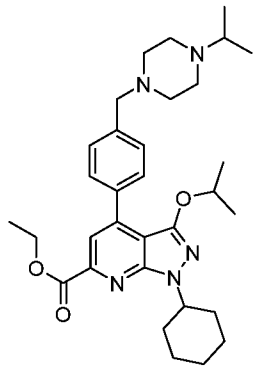
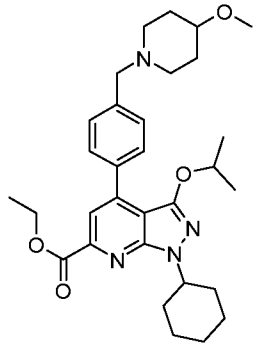
Int.	Structure	Name	SM	method	MW	Mes
E417		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-{1-[(oxan-4-yl)methyl]piperidin-4-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E413	I18	506	507
E418		methyl 3-cyclobutyl-4-{1-[(2,5-dimethoxyoxolan-3-yl)methyl]piperidin-4-yl}-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E413	I18	552	553
E419		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-[1-(3,3,3-trifluoropropyl)piperidin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E413	I18	504	505

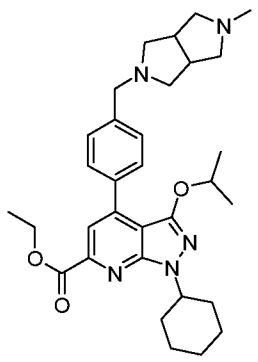
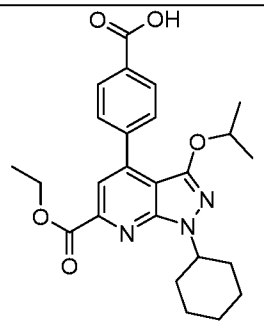
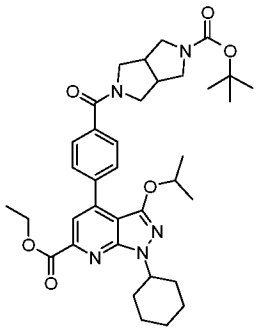
Int.	Structure	Name	SM	method	MW	Mes
E421		methyl 3-cyclobutyl-4-[1-(cyclopropylmethyl)piperidin-4-yl]-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E413	I18	462	463
E422		ethyl 1-(2-chloropyrimidin-4-yl)-3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E393	I5	525	526
E424		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP19	I3	521	522

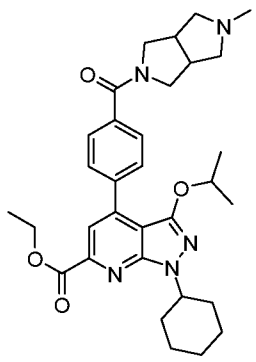
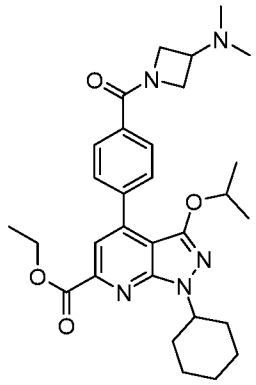
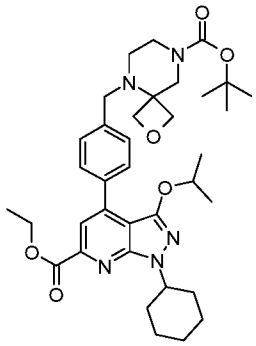
Int.	Structure	Name	SM	method	MW	Mes
E425		ethyl 1-cyclohexyl-4-(4-formylphenyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP36, AMP95	Specific example	435	436
E426		ethyl 1-cyclohexyl-4-(4-{[3-(dimethylamino)azetidin-1-yl]methyl}phenyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E425	I34, Specific example	519	520
E427		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(3-fluoropyrrolidin-1-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E353	I18	495	496

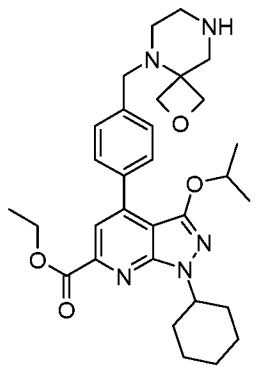
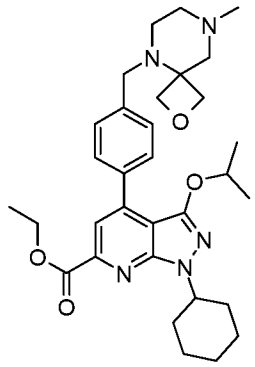
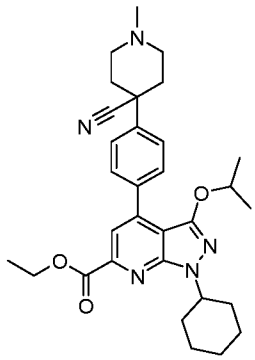
Int.	Structure	Name	SM	method	MW	Mes
E428		methyl 4-[4-(3-cyanoazetidin-1-yl)piperidin-1-yl]-3-cyclobutyl-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E353	I18	488	489
E429		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(3-methoxypyrrolidin-1-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E353	I18	507	508
E430		methyl 3-cyclobutyl-4-(1,4-dioxaspiro[4.5]dec-7-en-8-yl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP02	Specific example	445	446

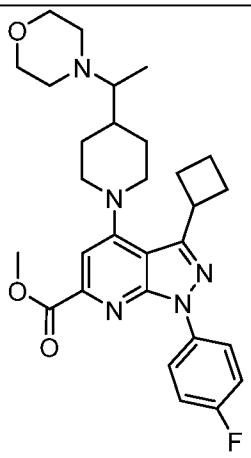
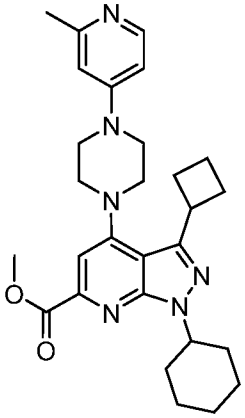
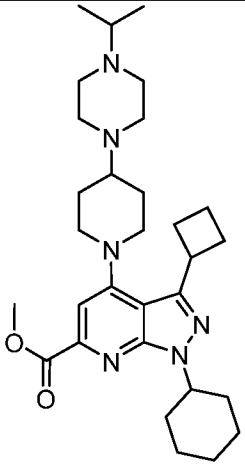
Int.	Structure	Name	SM	method	MW	Mes
E431		methyl 3-cyclobutyl-4-(1,4-dioxaspiro[4.5]decan-8-yl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E430	Specific example	447	448
E432		methyl 3-cyclobutyl-4-(4-oxocyclohexyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E431	Specific example	403	404
E433		methyl 3-cyclobutyl-4-[4-(morpholin-4-yl)cyclohexyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E432	I18	474	475

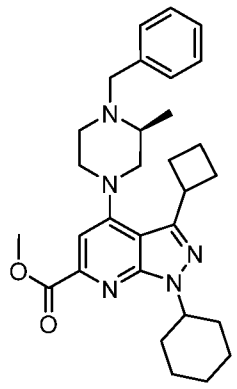
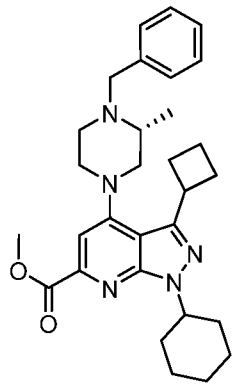
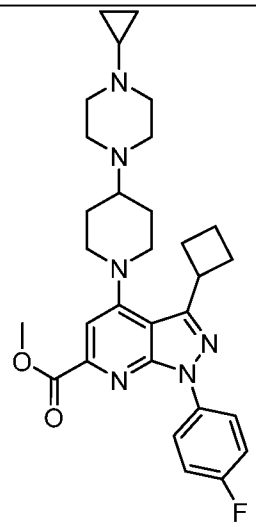
Int.	Structure	Name	SM	method	MW	Mes
E434		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[4-(propan-2-yl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E353	I18	534	535
E435		ethyl 1-cyclohexyl-3-[(propan-2-yl)oxy]-4-(4-{[4-(propan-2-yl)piperazin-1-yl]methyl}phenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E425	I34	547	548
E436		ethyl 1-cyclohexyl-4-{4-[(4-methoxypiperidin-1-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E425	I34	534	535

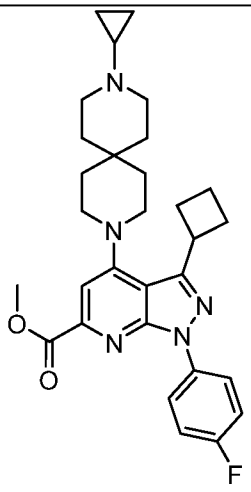
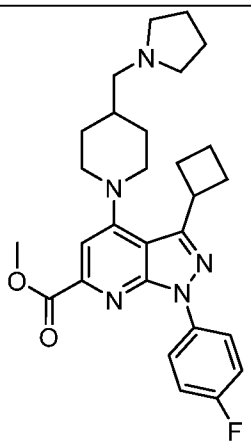
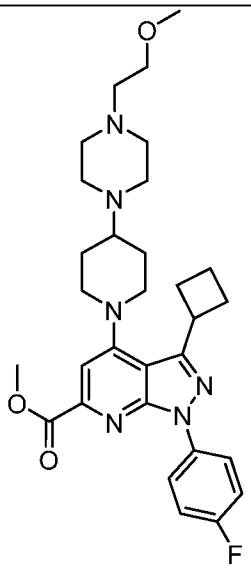
Int.	Structure	Name	SM	method	MW	Mes
E437		ethyl 1-cyclohexyl-4-{4-[(5-methylhexahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E425	I34	545	546
E438		4-{1-cyclohexyl-6-(ethoxycarbonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}benzoic acid	E425	Specific example	451	452
E439		ethyl 4-{4-[5-(*tert*-butoxycarbonyl)hexahydropyrrolo[3,4-*c*]pyrrole-2(1*H*)-carbonyl]phenyl}-1-cyclohexyl-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E438	I24, Specific example	645	646

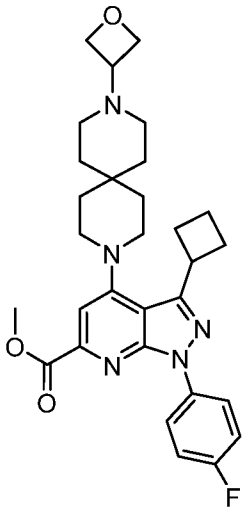
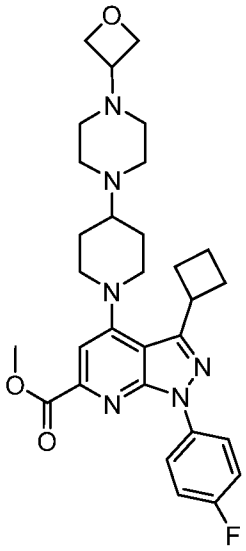
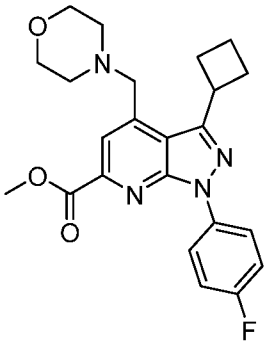
Int.	Structure	Name	SM	method	MW	Mes
E440		ethyl 1-cyclohexyl-4-[4-(5-methylhexahydropyrrolo[3,4-*c*]pyrrole-2(1*H*)-carbonyl)phenyl]-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E438	I24	559	560
E441		ethyl 1-cyclohexyl-4-{4-[3-(dimethylamino)azetidine-1-carbonyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E438	I24, Specific example	533	534
E442		ethyl 4-(4-{[8-(*tert*-butoxycarbonyl)-2-oxa-5,8-diazaspiro[3.5]nonan-5-yl]methyl}phenyl)-1-cyclohexyl-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E425	I34	647	648

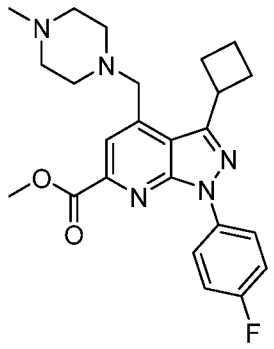
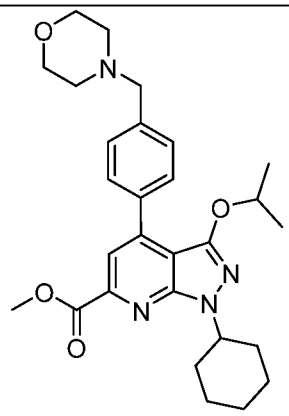
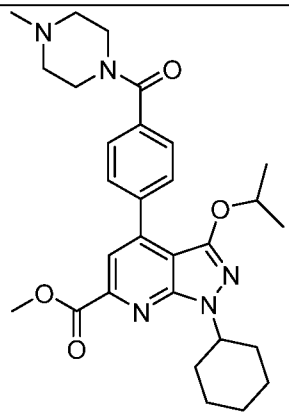
Int.	Structure	Name	SM	method	MW	Mes
E443		ethyl 1-cyclohexyl-4-{4-[(2-oxa-5,8-diazaspiro[3.5]nonan-5-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E442	I25	547	548
E444		ethyl 1-cyclohexyl-4-{4-[(8-methyl-2-oxa-5,8-diazaspiro[3.5]nonan-5-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E443	Specific example	561	562
E445		ethyl 4-[4-(4-cyano-1-methylpiperidin-4-yl)phenyl]-1-cyclohexyl-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	ALP38, AMP 95	Specific example	529	530

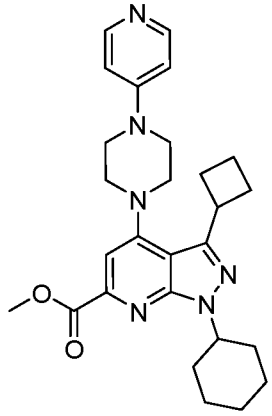
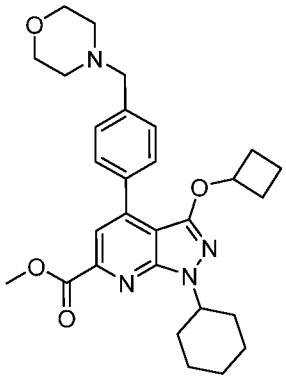
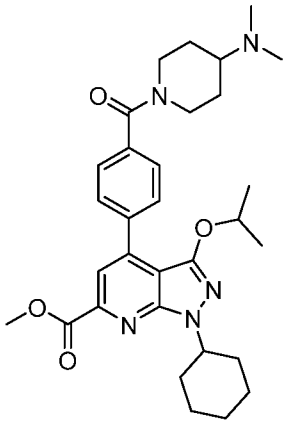
Int.	Structure	Name	SM	method	MW	Mes
E460		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[1-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP19, 436852-25-4	I3	521	522
E461		methyl 3-cyclobutyl-1-cyclohexyl-4-[4-(2-methylpyridin-4-yl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP25, 98010-38-9	I3	488	489
E462		methyl 3-cyclobutyl-1-cyclohexyl-4-{4-[4-(propan-2-yl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP25, 202991-78-4	I3	522	523

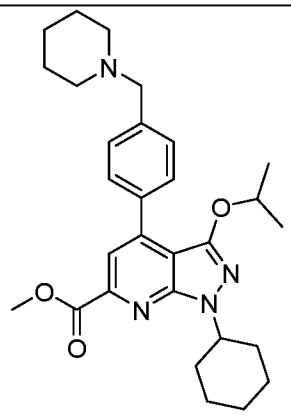
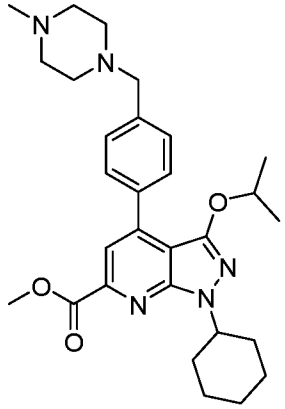
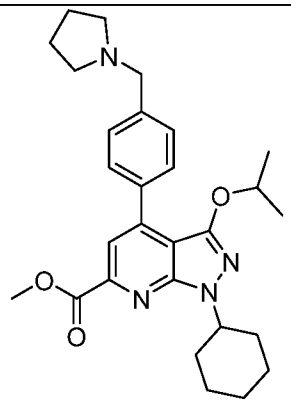
Int.	Structure	Name	SM	method	MW	Mes
E463		methyl 4-[(3*S*)-4-benzyl-3-methylpiperazin-1-yl]-3-cyclobutyl-1-cyclohexyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP25, 511254-92-57	I3	501	502
E464		methyl 4-[(3*R*)-4-benzyl-3-methylpiperazin-1-yl]-3-cyclobutyl-1-cyclohexyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP25, 158848 0-39-0	I3	501	502
E465		methyl 3-cyclobutyl-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E498	I26, Specific example	517	518

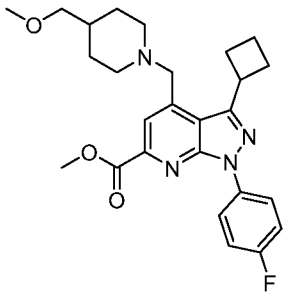
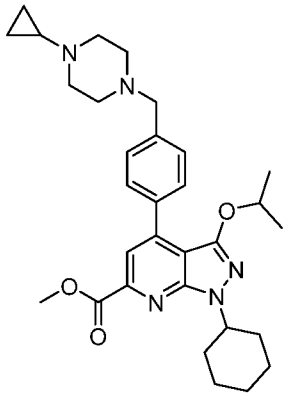
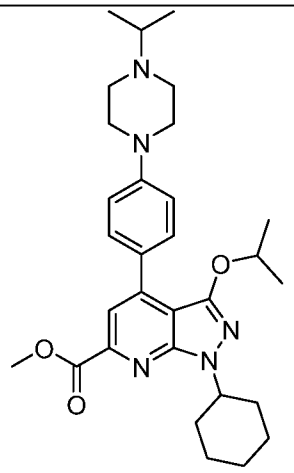
Int.	Structure	Name	SM	method	MW	Mes
E466		methyl 3-cyclobutyl-4-(9-cyclopropyl-3,9-diazaspiro[5.5]undecan-3-yl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E500	I26	517	518
E467		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP19, 683772-11-5	I3	491	492
E468		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[4-(2-methoxyethyl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E498, 6482-24-2	I27	550	551

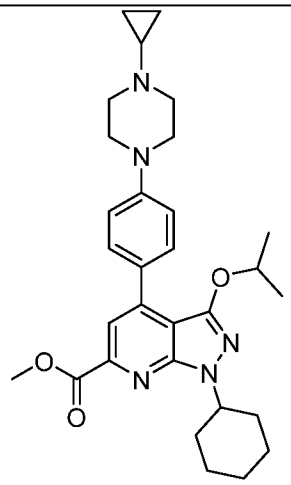
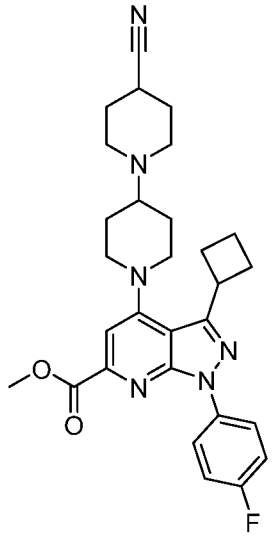
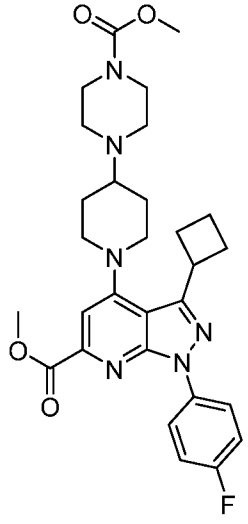
Int.	Structure	Name	SM	method	MW	Mes
E469		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-[9-(oxetan-3-yl)-3,9-diazaspiro[5.5]undecan-3-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E500, 6704-31-0	I30, Specific example	533	534
E470		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[4-(oxetan-3-yl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E498, 6704-31-0	I30	548	549
E471		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-[(morpholin-4-yl)methyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP19, 936329-94-1	J13	424	425

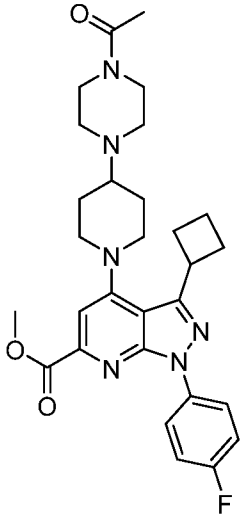
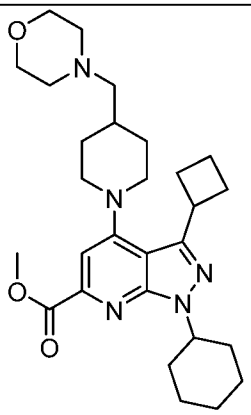
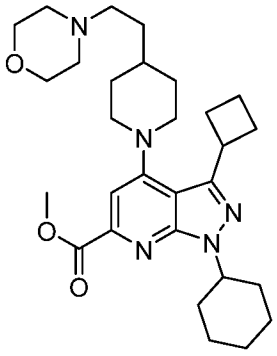
Int.	Structure	Name	SM	method	MW	Mes
E472		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-[(4-methylpiperazin-1-yl)methyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP19, 1015484-22-6	J13	438	439
E473		methyl 1-cyclohexyl-4-{4-[(morpholin-4-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E504, 1268340-94-8	J13	493	493
E474		methyl 1-cyclohexyl-4-[4-(4-methylpiperazine-1-carbonyl)phenyl]-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E504, 34352-59-5	I28, Specific example	519	520

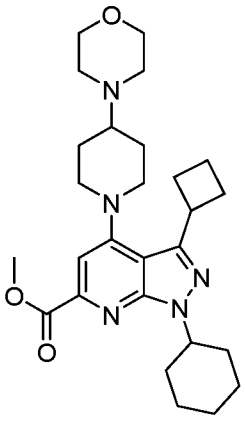
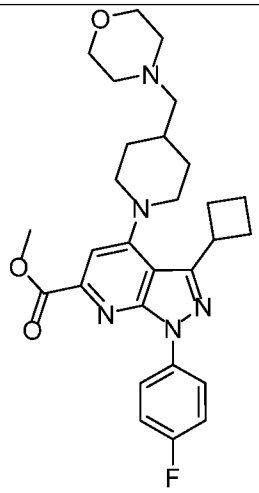
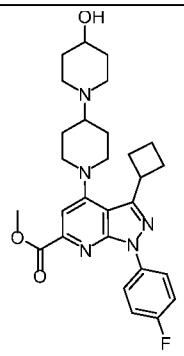
Int.	Structure	Name	SM	method	MW	Mes
E475		methyl 3-cyclobutyl-1-cyclohexyl-4-[4-(pyridin-4-yl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP25, 1008-91-9	I3	474	475
E476		methyl 3-(cyclobutyloxy)-1-cyclohexyl-4-{4-[(morpholin-4-yl)methyl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E505, 1268340-94-8	J13	504	505
E477		methyl 1-cyclohexyl-4-{4-[4-(dimethylamino)piperidine-1-carbonyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E504, 4318-42-7	I28	548	549

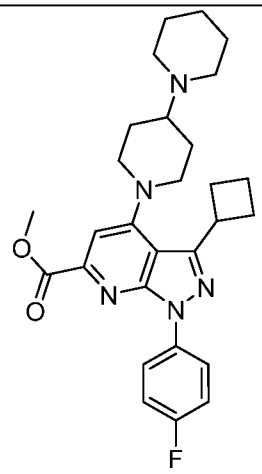
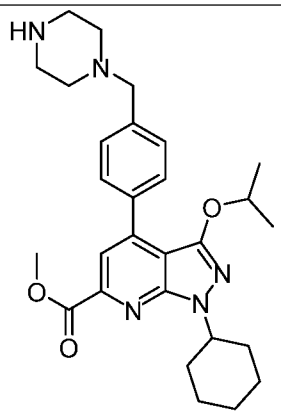
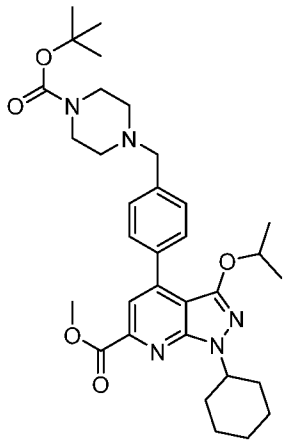
Int.	Structure	Name	SM	method	MW	Mes
E478		methyl 1-cyclohexyl-4-{4-[(piperidin-1-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E504, 1268340-93-7	J13	491	492
E479		methyl 1-cyclohexyl-4-{4-[(4-methylpiperazin-1-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E504, 1015484-22-6	J13	506	507
E480		methyl 1-cyclohexyl-3-[(propan-2-yl)oxy]-4-{4-[(pyrrolidin-1-yl)methyl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E504, 888711-53-3	J13	477	477

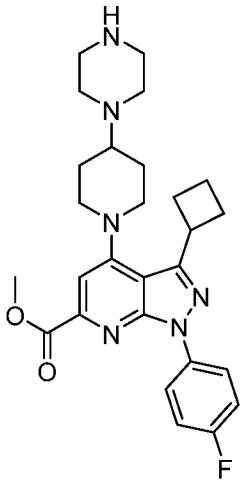
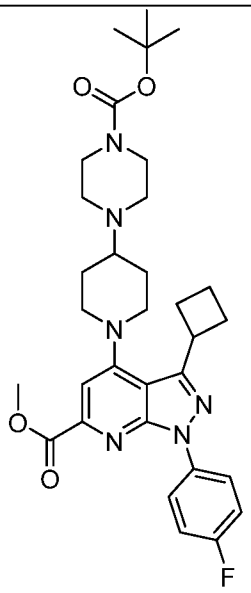
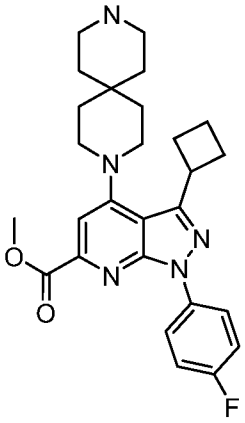
Int.	Structure	Name	SM	method	MW	Mes
E481		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-{[4-(methoxymethyl)piperidin-1-yl]methyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP19, BF01	J13	466	467
E482		methyl 1-cyclohexyl-4-{4-[(4-cyclopropylpiperazin-1-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E494	I26	531	532
E483		methyl 1-cyclohexyl-3-[(propan-2-yl)oxy]-4-{4-[4-(propan-2-yl)piperazin-1-yl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E504, 4318-42-7	I29	519	520

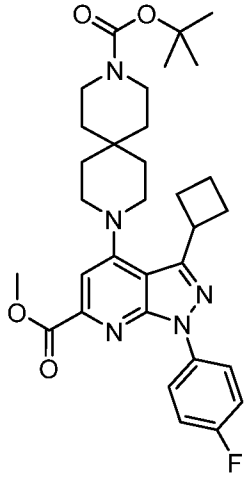
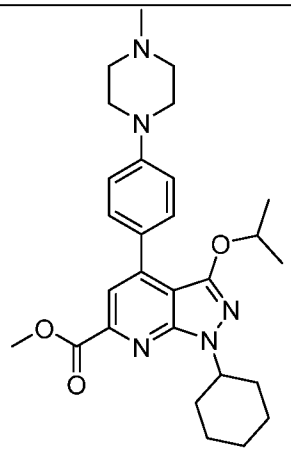
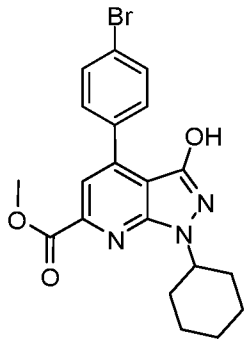
Int.	Structure	Name	SM	method	MW	Mes
E484		methyl 1-cyclohexyl-4-[4-(4-cyclopropylpiperazin-1-yl)phenyl]-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E504, 20327-23-5	I29	517	518
E485		methyl 4-(4-cyano[1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP19, AMI11	I3	516	517
E486		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[4-(methoxycarbonyl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E498	I31, Specific example	550	551

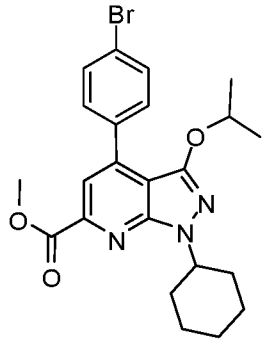
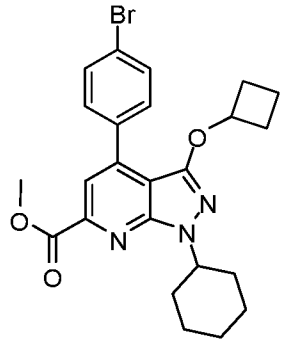
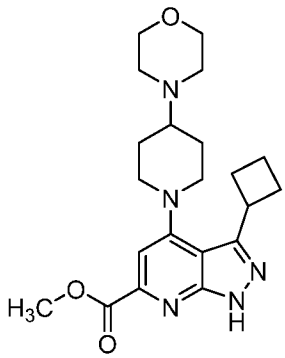
Int.	Structure	Name	SM	method	MW	Mes
E487		methyl 4-[4-(4-acetylpiperazin-1-yl)piperidin-1-yl]-3-cyclobutyl-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E498	I32, Specific example	534	535
E488		methyl 3-cyclobutyl-1-cyclohexyl-4-{4-[(morpholin-4-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP25, 81310-62-5	I3	495	496
E489		methyl 3-cyclobutyl-1-cyclohexyl-4-{4-[2-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP25, 500357-64-2	I3	509	510

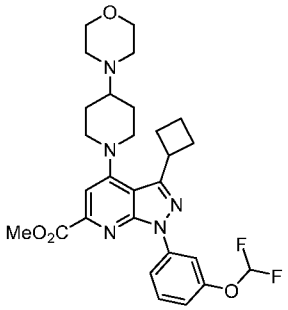
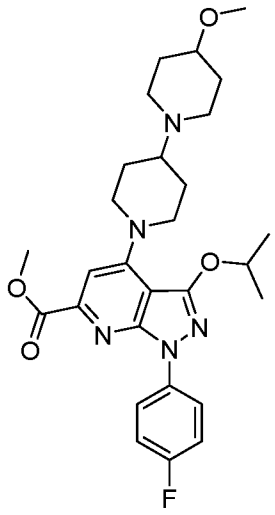
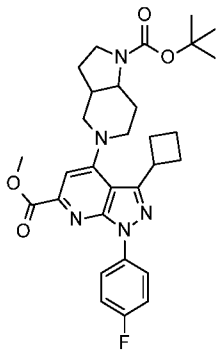
Int.	Structure	Name	SM	method	MW	Mes
E490		methyl 3-cyclobutyl-1-cyclohexyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP25, 53617-35-9	I3	481	482
E491		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[(morpholin-4-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP19, 202991-78-4	I3	507	508
E492		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-(4-hydroxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP19, 202991-78-4	I3	507	508

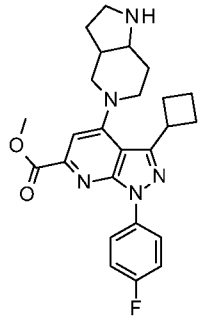
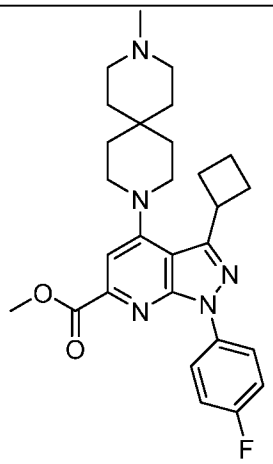
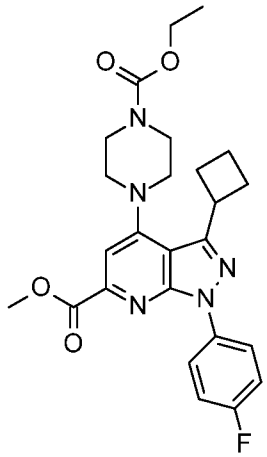
Int.	Structure	Name	SM	method	MW	Mes
E493		methyl 4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP19, 202991-78-4	I3	491	492
E494		methyl 1-cyclohexyl-4-{4-[(piperazin-1-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E495	I25	491	492
E495		methyl 4-(4-{[4-(*tert*-butoxycarbonyl)piperazin-1-yl]methyl}phenyl)-1-cyclohexyl-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E504, 936329-97-4	J13	591	592

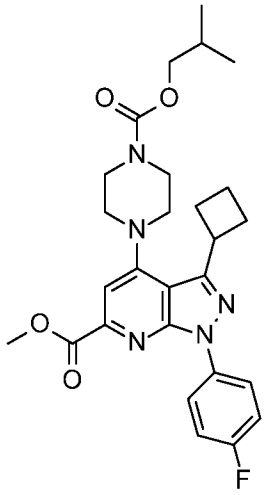
Int.	Structure	Name	SM	method	MW	Mes
E498		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(piperazin-1-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E499	I25	492	493
E499		methyl 4-{4-[4-(*tert*-butoxycarbonyl)piperazin-1-yl]piperidin-1-yl}-3-cyclobutyl-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP19, 205059-24-1	I3	592	593
E500		methyl 3-cyclobutyl-4-(3,9-diazaspiro[5.5]undecan-3-yl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E501	I25	477	478

Int.	Structure	Name	SM	method	MW	Mes
E501		*tert*-butyl 9-[3-cyclobutyl-1-(4-fluorophenyl)-6-(methoxycarbonyl)-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl]-3,9-diazaspiro[5.5]undecane-3-carboxylate	HP19173405-78-2	I3	577	578
E502		methyl 1-cyclohexyl-4-[4-(4-methylpiperazin-1-yl)phenyl]-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E504, 109-01-3	I29, Specific example	491	492
E503		methyl 4-(4-bromophenyl)-1-cyclohexyl-3-hydroxy-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	436088-86-7 and 608128-34-3	I1, Specific example	430	431

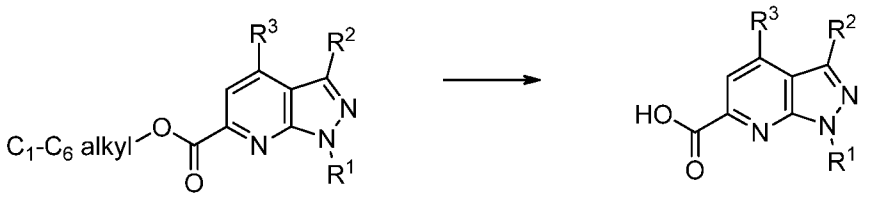
Int.	Structure	Name	SM	method	MW	Mes
E504		methyl 4-(4-bromophenyl)-1-cyclohexyl-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E503	I17, Specific example	472	472
E505		methyl 4-(4-bromophenyl)-3-(cyclobutyloxy)-1-cyclohexyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E503	I17, Specific example	504	505
E509		methyl 3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	53617-35-9, 16063-69-7, 5006-22-4, 301-01-2, 630-08-0	Specific example	399	400

Int.	Structure	Name	SM	method	MW	Mes
E510		methyl 3-cyclobutyl-1-[3-(difluoromethoxy)phenyl]-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E509	I7, Specific example	541	542
E511		methyl 1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	AMP96	Specific example	525	526
E513		methyl 4-[1-(*tert*-butoxycarbonyl)octahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl]-3-cyclobutyl-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylatee	HP19	I3	549	550

Int.	Structure	Name	SM	method	MW	Mes
E514		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-(octahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	E513	I21A	449	450
E515		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-(9-methyl-3,9-diazaspiro[5.5]undecan-3-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP19, 13323-45-0	I3	491	492
E516		methyl 3-cyclobutyl-4-[4-(ethoxycarbonyl)piperazin-1-yl]-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP19, 120-43-4	I3	481	482

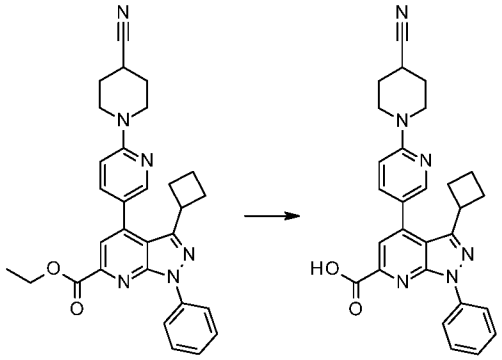
Int.	Structure	Name	SM	method	MW	Mes
E517		methyl 3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[(2-methylpropoxy)carbonyl]piperazin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate	HP19, 23672-96-0	I3	509	510

Method J1: Synthesis of carboxylic acids by saponification of ester



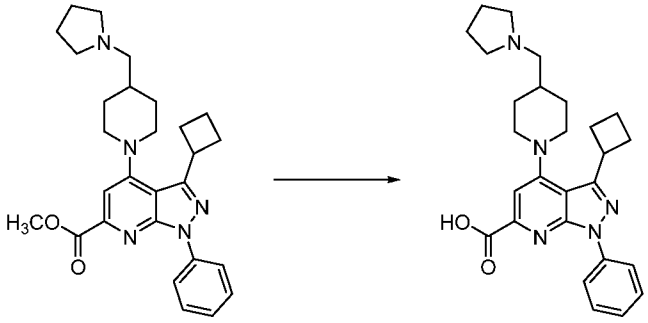
[00650] To the intermediate ester (1 equiv) in THF or in a mixture of THF/methanol or in dioxane/water or in THF/methanol/water at RT is added either aqueous 1 to 2 N sodium hydroxide or lithium hydroxide monohydrate (from 1 to 5 equiv). The reaction mixture is stirred at a temperature ranging from RT to 60 °C for 20 minutes to several days (up to 8 days). The volatiles are removed under reduced pressure, and the resulting mixture is acidified with either aqueous 2-6 N HCl or acetic acid. If a filterable suspension is obtained, the precipitate is collected by filtration, washed with water and dried in vacuo to afford the titled compound which is used as such or further purified either by preparative HPLC or flash chromatography on silica gel. In other cases, the mixture is partitioned between water and either dichloromethane or ethyl acetate. The two phases are separated, and the aqueous phase is optionally neutralized and then extracted either with dichloromethane or ethyl acetate. The combined organic phases are washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to afford the titled compound which is used as such or further purified either by preparative HPLC or flash chromatography on silica gel.

Illustrative synthesis of intermediate A056: 4-(4-Cyano-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-5'-yl)-3-cyclobutyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxylic acid



[00651] Intermediate E018 (30.7g, 60.3 mmol) was dissolved in a mixture of THF/methanol (1/1; 1 L) and 2 N sodium hydroxide (109 mL, 218 mmol) in water was added at RT. The solution was stirred for 1 hour. The volatiles were removed under reduced pressure, and the resulting mixture was diluted with water (300 mL). The aqueous phase was acidified with aqueous 2 N HCl (110 mL), and the precipitate was filtered, washed with water and dried at 40 °C under reduced pressure to give the titled compound.

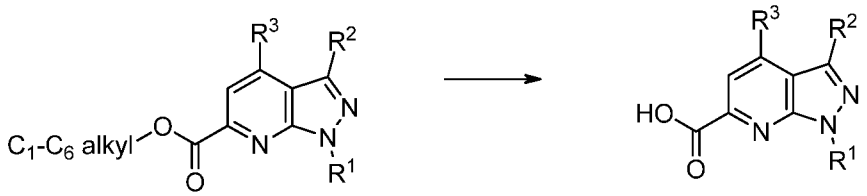
Illustrative synthesis of intermediate A285: 3-cyclobutyl-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1H-pyrazolo[3,4-b]pyridine-6-carboxylic acid



[00652] Methyl 3-cyclobutyl-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate (18.39 g, 38.8 mmol, E357) was dissolved in a mixture of tetrahydrofuran (100 mL), methanol (50 mL), and water (100 mL). To this mixture was added lithium hydroxide hydrate (4.89 g, 116 mmol). The resulting suspension was heated at 50 °C for 30 minutes. The reaction mixture was cooled to room temperature and neutralized with 6 M aqueous HCl (6 mL) to a pH of 7. To this was then added water in 10 mL portions. After a total of 200 mL of water had been added, a solid formed. The solid was collected by filtration and

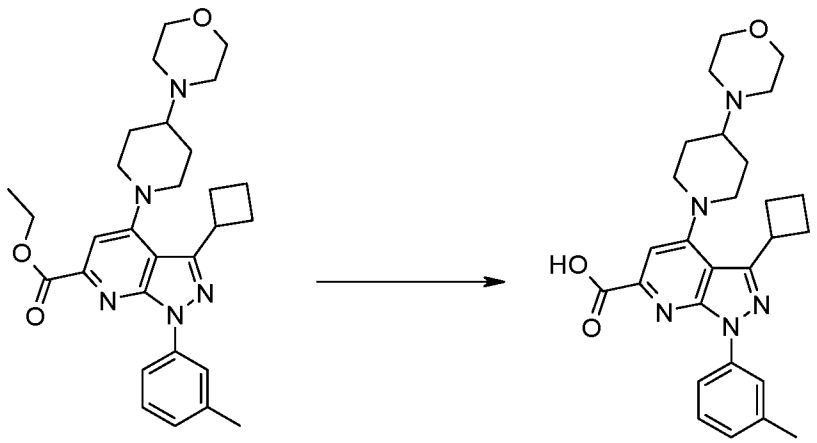
dried to constant weight in a vacuum oven at 50 °C over 72 hours to give 14.98 g of the titled compound. ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.89 (d, J = 8.0 Hz, 2H), 7.84 (s, 1H), 7.52 (t, J = 7.9 Hz, 2H), 7.25 (t, J = 7.5 Hz, 1H), 4.14 (p, J = 8.4 Hz, 1H), 3.56 (dd, J = 12.2, 3.7 Hz, 2H), 2.86 - 2.67 (m, 4H), 2.63 (br s, 4H), 2.53 - 2.42 (m, 4H), 2.10 – 1.98 (m, 4H), 1.83 – 1.68 (m, 5H), 1.63 – 1.48 (m, 2H); MS (ESI+) *m/z* 460.2 $(M+H)^+$.

Method J1A: Synthesis of carboxylic acids by saponification of ester



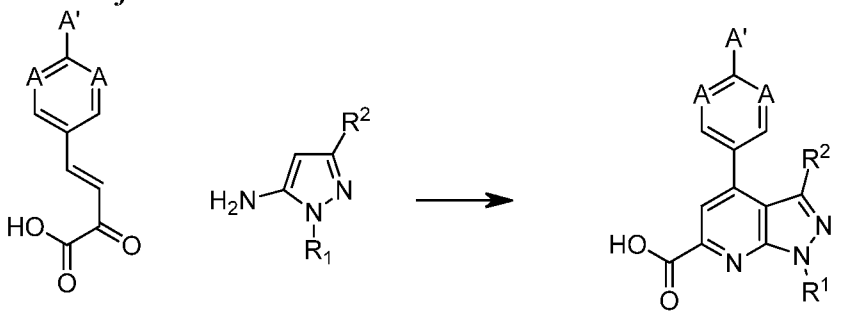
[00653] To the ester intermediate (1 equiv) in THF or ethanol or methanol or a mixture of the cited solvents at RT is added either aqueous 1 N or 2 N sodium hydroxide 1 (from 1 to 10 equiv). The reaction mixture is stirred at RT until complete conversion is observed. Sodium hydroxide can be added to allow the full conversion of the starting ester. The volatiles are removed under reduced pressure, and the resulting mixture is acidified with either aqueous 1 N or 2 N HCl. If a filterable suspension is obtained, the precipitate is collected by filtration, washed with water and dried in vacuo to afford the titled compound which is used as such or further purified either by preparative HPLC or flash chromatography on silica gel. In other cases, the mixture is partitioned between a phosphate buffer (pH 6.2) and either dichloromethane or chloroform or a mixture of dichloromethane/isopropanol. The organic phases are separated, dried over $MgSO_4$, filtered and concentrated in vacuo to afford the titled compound which is used as such or further purified either by preparative HPLC or flash chromatography on silica gel.

*Illustrative synthesis of A318a: 3-cyclobutyl-1-(3-methylphenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid*



[00654] Ester E395 (40 mg, 80 µmol) was dissolved in a mixture of THF/ethanol (1/1; 6 mL) and 1 N sodium hydroxide (0.5 mL, 500 µmol) in water was added at RT. The solution was stirred for 4 hours. Aqueous 1 N HCl (0.5 mL, 500 µmol) and a phosphate buffer were added (pH 6.2). The solvent was partially removed under reduced pressure, and the resulting mixture was extracted twice with chloroform. The combined organic phases were dried over magnesium sulfate, filtered and evaporated under reduced pressure to give the titled compound.

Method J2: Synthesis of acids



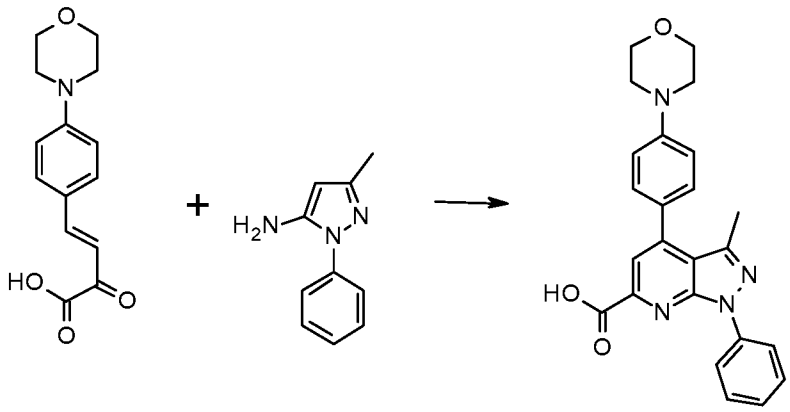
A is either N or CH

A' is either R^e or L^1-G^{3C} as described in the Summary

[00655] The alkylidene pyruvate (1 to 1.5 equiv) and the aminopyrazole (1 to 1.5 equiv) in acetic acid are stirred under air at temperatures ranging from RT to reflux for 1 h to several days. Alternatively, the alkylidene pyruvate (1 to 1.5 equiv) and the aminopyrazole (1 to 1.5 equiv) in DMF or acetic acid are heated under microwave irradiation at 150 °C for 20 minutes to 2 h followed by stirring under air in an opened flask at temperatures ranging from RT to 90 °C for 1 h to several days with or without dilution of the reaction mixture with a large amount of ethanol or methanol. Then the reaction mixture is filtered, and the solid is washed with solvents, and

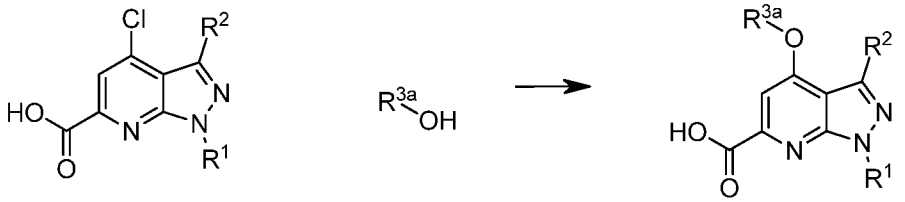
dried in vacuo to afford the titled compound which is used as such or purified by precipitation, by preparative HPLC or by flash chromatography on silica gel. Alternatively, the reaction mixture is concentrated in vacuo to afford a crude mixture which is used as such or further purified either by precipitation, by preparative HPLC or by flash chromatography on silica gel.

Illustrative synthesis of intermediate A002: 3-methyl-4-(4-morpholinophenyl)-1-phenyl-pyrazolo[3,4-b]pyridine-6-carboxylic acid



[00656] ALP01 (261 mg, 1 mmol, 1 equiv) and 3-methyl-1-phenyl-1*H*-pyrazol-5-amine (CAS 1131-18-6, 173mg, 1 mmol, 1 equiv) were introduced in a sealed tube. DMF (2 mL) was added, and the vial was sealed. The reaction mixture was heated under microwave irradiation at 150 °C for 1 h. Then after cooling down to RT, the vial was opened, diluted with a large amount of ethanol, and stirred vigorously under air at RT overnight. The resulting suspension was filtered. The solid was washed with ethanol, and dried in vacuo to afford the titled compound.

Method J3: Nucleophilic substitution on the central core with alcohols

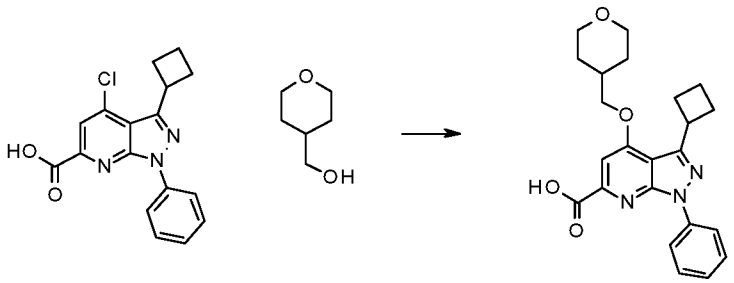


[00657] To a solution of alcohol (3.0 equiv) in anhydrous THF under nitrogen atmosphere at RT is added 60% sodium hydride in mineral oil (6.0 equiv), and the mixture is stirred at room temperature for 30 minutes. Then the aryl chloride intermediate HP (1.0 equiv) is added, the reaction mixture is stirred at room temperature for 5 minutes, and then heated at reflux for 1 h to

24 h. The reaction mixture is cooled to 0 °C, diluted with heptane, quenched with water and acidified with 2 N HCl (6.0 equiv). Volatiles are removed in vacuo. The resulting aqueous residue is filtered, and the solid is washed with water and with a mixture heptane/Et_2O 1/1, and dried in vacuo to afford the titled compound which is used as such or purified by silica gel chromatography. Alternatively, the aqueous residue is diluted with dichloromethane. The two phases are separated and the aqueous phase is extracted with dichloromethane. The combined organic phases are washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to afford the titled compound which is used as such or purified by silica gel chromatography.

[00658] Alternatively, to a solution of alcohol (2.0 equiv) in anhydrous DMF is added 1 M potassium *tert*-butoxide (3-4 equiv), and the mixture is stirred at room temperature for several minutes. Then the aryl chloride intermediate HP (1.0 equiv) is added, and then the reaction mixture is heated at 40-60 °C for 1 h to 24 h. After cooling to ambient temperature, the product can be precipitated from an appropriate solvent or purified chromatographically.

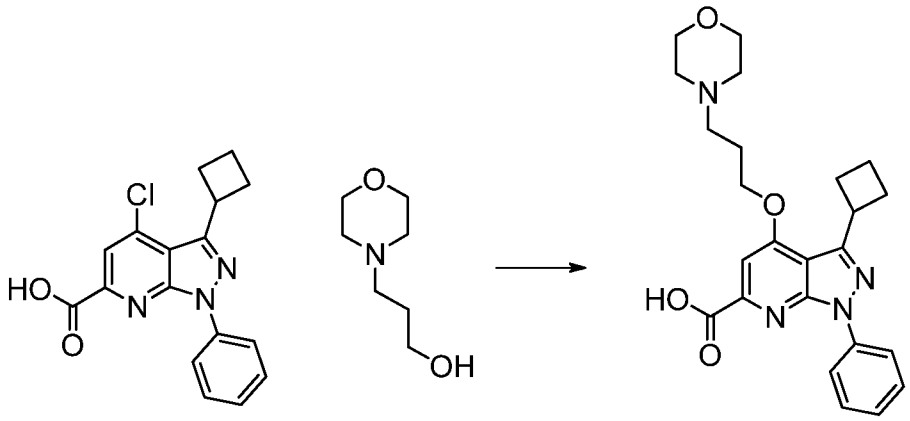
Illustrative synthesis of intermediate A148: 3-cyclobutyl-1-phenyl-4-(tetrahydropyran-4-ylmethoxy)pyrazolo[3,4-b]pyridine-6-carboxylic acid



[00659] To a solution of tetrahydropyran-4-ylmethanol (CAS: 14774-37-9, 54 mg, 0.457 mmol, 3.0 equiv) in anhydrous THF (1 mL) under nitrogen atmosphere was added 60% sodium hydride in mineral oil (37 mg, 0.915 mmol, 6.0 equiv), and the mixture was stirred at room temperature for 30 minutes. HP10 (50 mg, 0.152 mmol, 1.0 equiv) was added; the reaction mixture was stirred at room temperature for 5 minutes and then heated at reflux for 3 hours. The reaction mixture was cooled to 0 °C, diluted with heptane (1 mL), quenched with water (1 mL) and acidified with 2 N HCl (0.46 mL, 6.0 equiv). Volatiles were removed in vacuo. The resulting aqueous suspension was diluted with a mixture heptane/Et_2O: 1/1 (1 mL) and filtered. The solid was washed with water and with a mixture heptane/Et_2O 1/1 and dried in vacuo. The crude solid was purified by silica gel chromatography (eluent system:

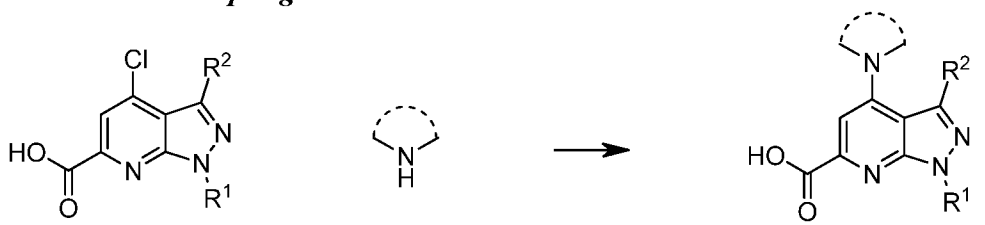
DCM/(DCM/MeOH/AcOH/H_2O: 90/10/1/1) gradient from 100/0 to 90/10) to give the titled compound.

Illustrative synthesis of intermediate A173: 3-cyclobutyl-4-(3-morpholinopropoxy)-1-phenyl-pyrazolo[3,4-b]pyridine-6-carboxylic acid



[00660] 3-Morpholinopropan-1-ol (73 mg, 0.50 mmol) was dissolved into anhydrous DMF (830 µL), treated with 1 M KOtBu in THF (830 µL, 0.83 mmol), stirred three minutes, treated further with intermediate HP10 (82 mg, 0.25 mmol), and heated at 50 °C for about an hour. More DMF (570 µL) was added and heating was continued overnight. The mixture was brought to room temperature, diluted with MeCN and filtered with a MeCN rinse. The collected solids were mixed with acetic acid into DMSO, and diluted with water to precipitate solids which were collected by filtration, rinsed with water and dried under vacuum to give the titled compound (65 mg). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.38-8.28 (m, 2H), 7.61-7.52 (m, 2H), 7.41 (s, 1H), 7.36-7.29 (m, 1H), 4.43-4.34 (m, 2H), 4.08-3.98 (m, 1H), 3.62-3.58 (m, 4H), 2.57-2.35 (m, 10H), 2.15-1.89 (m, 4H).

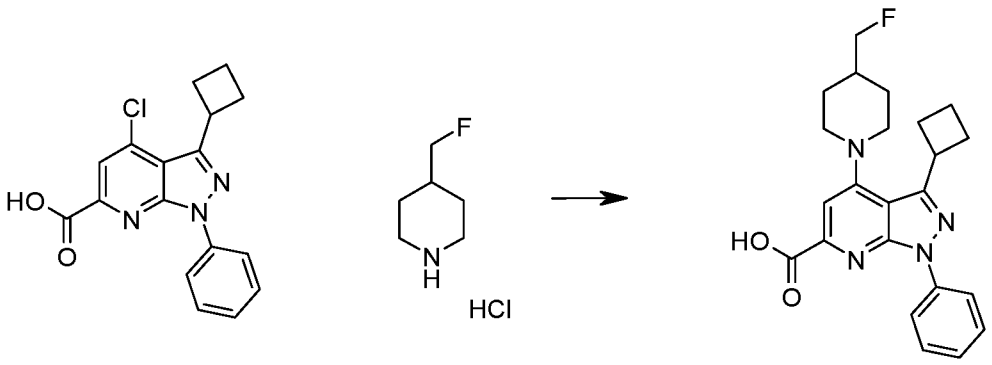
Method J4: Buchwald coupling on the central core



[00661] To a degassed solution of the aryl chloride intermediate HP (1.0 equiv) and the amine as free base or hydrochloride salt (1.5 equiv) in anhydrous THF at RT under nitrogen atmosphere in a sealed vial is added XPhos Pd G1 (CAS 1028206-56-5, 0.1 equiv) followed by 1 N

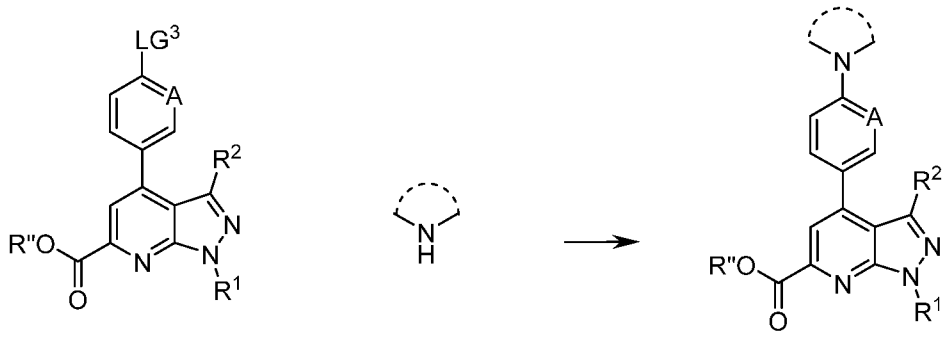
LiHMDS in THF (from 3 to 5 equiv). The reaction mixture is purged with nitrogen and the vial is sealed. The reaction mixture is stirred at 100 °C for 1 h to 24 h. Then the reaction mixture is cooled down and volatiles are removed in vacuo. The resulting residue is taken up in dichloromethane and water and acidified with acetic acid. The two phases are separated and the aqueous phase is extracted with dichloromethane. The combined organic layers are washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting residue is purified by flash chromatography on silica gel to afford the titled compound.

Illustrative synthesis of intermediate A216: 3-cyclobutyl-4-[4-(fluoromethyl)-1-piperidyl]-1-phenyl-pyrazolo[3,4-b]pyridine-6-carboxylicacid



[00662] To a degassed solution of HP10 (64 mg, 0.194 mmol, 1.0 equiv) and 4-(fluoromethyl)piperidine hydrochloride (CAS 259143-04-9, 45mg, 0.292 mmol, 1.5 equiv) in anhydrous THF (2 mL) at RT under nitrogen atmosphere in a sealed vial was added XPhos Pd G1 (CAS 1028206-56-5, 14 mg, 0.019 mmol, 0.1 equiv) followed by 1 N LiHMDS in THF (0.97 mL, 0.97 mmol, 5.0 equiv). The reaction mixture was purged with nitrogen, and the vial was sealed. The reaction mixture was stirred at 100 °C overnight. Then the reaction mixture was cooled down and volatiles were removed in vacuo. The resulting residue was taken up in dichloromethane and water and acidified with acetic acid. The two phases were separated, and the aqueous phase was extracted with dichloromethane. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting residue was purified by flash chromatography on silica gel (eluent system: dichloromethane/methanol gradient from 100/0 to 95/5) to afford the titled compound.

Method J5: Buchwald coupling on the aryl linker



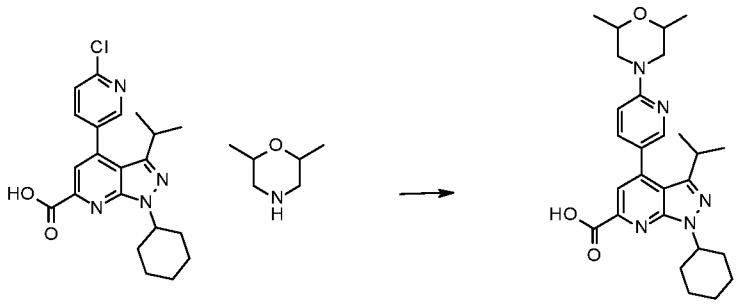
R" = H or C_1-C_6 alkyl

A = N or CH

LG^3 = Cl or Br

[00663] To a degassed solution of pyridyl chloride (1.0 equiv) and amine (1.5 equiv) in anhydrous THF at RT under nitrogen atmosphere is added 1 N LiHMDS in THF (from 3 to 4.5 equiv) followed by XPhos Pd G1 (CAS 1028206-56-5, 0.1 equiv). The reaction mixture is stirred at room temperature for 1 h to 24 h. The mixture is quenched with acetic acid and diluted with water and dichloromethane. The organic layer is separated, washed with water and brine, dried over $MgSO_4$, filtered and concentrated in vacuo to afford the titled compound which is used as such or further purified by preparative HPLC or by flash chromatography on silica gel. The cross-coupling reaction can be performed on either a carboxylic acid or ester. In some instances, an ester starting material is concomitantly hydrolyzed to the corresponding carboxylic acid product under the reaction conditions.

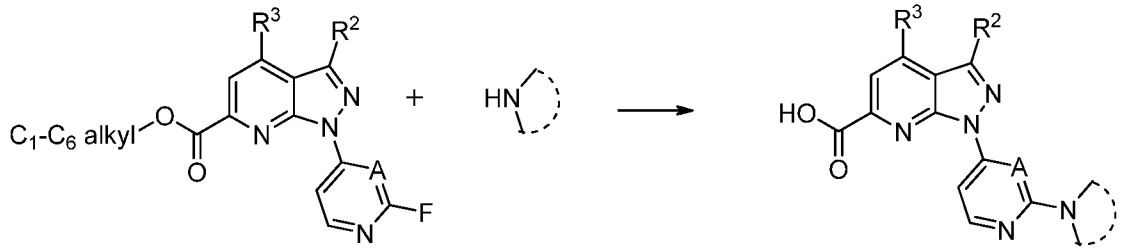
Illustrative synthesis of intermediate A065: 1-cyclohexyl-4-[6-(2,6-dimethylmorpholin-4-yl)-3-pyridyl]-3-isopropyl-pyrazolo[3,4-b]pyridine-6-carboxylic acid



[00664] To a degassed solution of A250 (75 mg, 0.188 mmol, 1.0 equiv) and 2,6-dimethylmorpholine (CAS 141-91-3, 32 µL, 0.26 mmol, 1.5 equiv) in anhydrous THF (0.7 mL)

at RT under nitrogen atmosphere was added 1 N LiHMDS in THF (765 µL, 0.765 mmol, 4.5 equiv) followed by XPhos Pd G1 (CAS 1028206-56-5, 12.5 mg, 0.017 mmol, 0.1 equiv). The reaction mixture was stirred at room temperature for 1 h. The mixture was quenched with AcOH and diluted with water and dichloromethane. The organic layer was separated, washed with water and brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting residue was purified by silica gel chromatography (eluent system: dichloromethane/methanol, gradient from 100/0 to 95/5) to afford the titled compound.

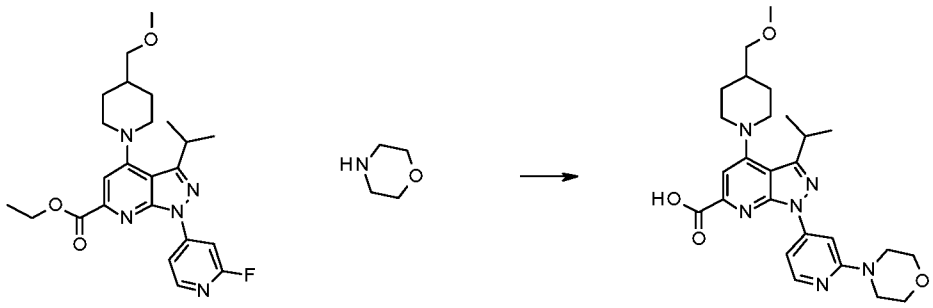
Method J6: Nucleophilic substitution on the R^1 part



A = N or CH

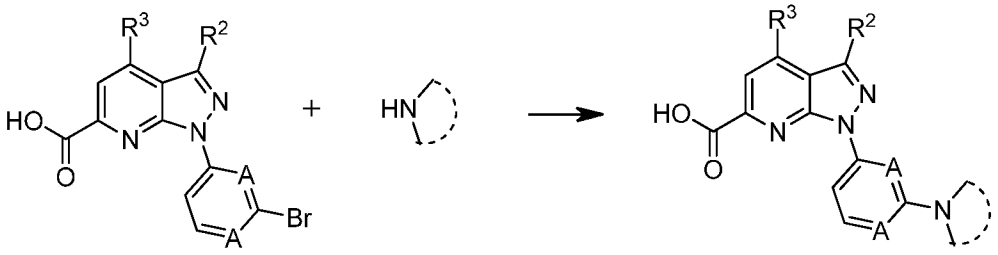
[00665] To the intermediate fluoropyridine (1.0 equiv) in anhydrous DMSO is added the amine (from 2.0 to 10.0 equiv) and K_2CO_3 (from 3.0 to 10 equiv). The reaction mixture is stirred at 100 °C overnight. If the reaction is not complete, additional amine (from 2.0 to 10 equiv) and K_2CO_3 (from 0 to 10 equiv) are added, and the reaction mixture is stirred at 100 °C until the reaction is finished. Then the reaction mixture is cooled down to RT, diluted with water and extracted with ethyl acetate. The combined organic layers are washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to afford the titled compound which is used as such or purified by flash chromatography on silica gel.

Illustrative synthesis of intermediate A179: 3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]-1-(2-morpholino-4-pyridyl)pyrazolo[3,4-b]pyridine-6-carboxylic acid



[00666] To E147 (144 mg, 0.32 mmol, 1.0 equiv) in anhydrous DMSO (1.5 mL) was added morpholine (56 µL, 0.64 mmol, 2.0 equiv) and K_2CO_3 (133 mg, 0.96 mmol, 3.0 equiv). The reaction mixture was stirred at 100 °C overnight. Additional morpholine (56 µL, 0.64 mmol, 2.0 equiv) and K_2CO_3 (133 mg, 0.96 mmol, 3.0 equiv) were added, and the reaction mixture was stirred at 100 °C for 24 h. Then additional morpholine (56 µL, 0.64 mmol, 2.0 equiv) was added again, and the reaction mixture was stirred at 100 °C for 5 days. Then the reaction mixture was cooled down to RT, diluted with water and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting residue was purified by silica gel chromatography (eluent system: dichloromethane/methanol, gradient 100/0 to 95/5 with 0.1% AcOH) to afford the titled compound.

Method J7: Buchwald coupling on the phenyl or heteroaryl halogen

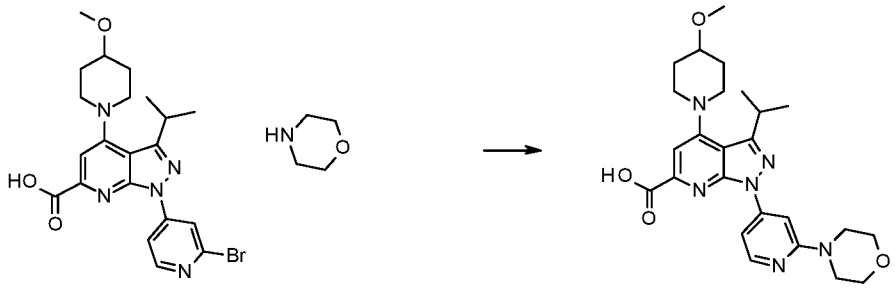


A = CH, N

[00667] To a degassed solution of the aromatic bromide intermediate (1.0 equiv) and the amine as free base or hydrochloride salt (from 1.5 to 2 equiv) in anhydrous THF at RT under nitrogen atmosphere in a sealed vial is added XPhos Pd G1 (CAS 1028206-56-5, 0.1 equiv) followed by 1 N LiHMDS in THF (from 3 to 5 equiv). The reaction mixture is purged with nitrogen, and the vial is sealed. The reaction mixture is stirred at a temperature ranging from RT to 100 °C for 1 h to 3 h. If the reaction is not complete, additional amine (from 1.0 to 3.0 equiv),

LiHMDS (from 1.5 to 6.0 equiv) and XPhos Pd G1 (CAS 1028206-56-5, from 0.05 to 0.2 equiv) are added at RT. The reaction mixture is purged again with nitrogen and the vial is sealed. The reaction mixture is stirred at a temperature ranging from RT to 100 °C for 1 h to 3 h. Then the reaction mixture is cooled down and volatiles are removed in vacuo. The resulting residue is taken up in dichloromethane and water and acidified with acetic acid. The two phases are separated, and the aqueous phase is extracted with dichloromethane. The combined organic layers are washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting residue is purified by flash chromatography on silica gel to afford the titled compound.

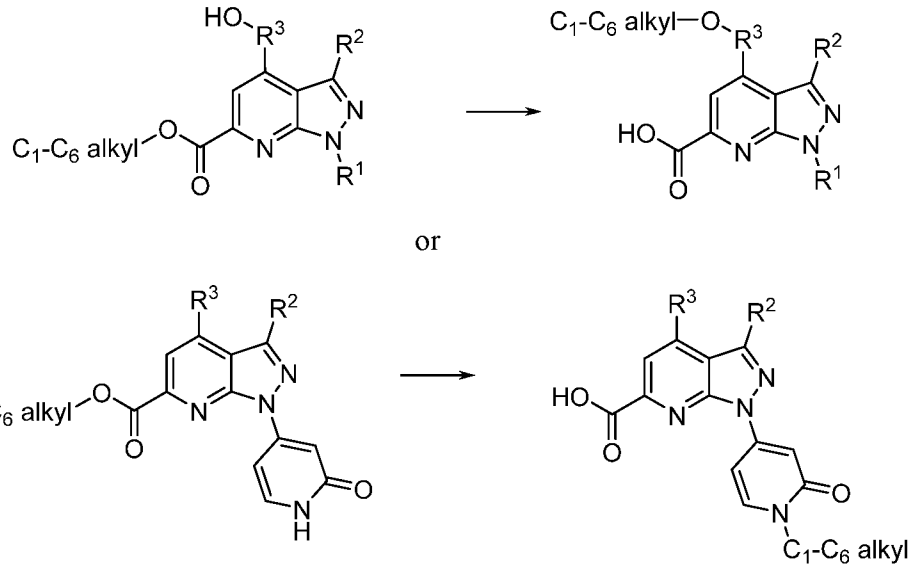
Illustrative synthesis of intermediate A212: 3-isopropyl-4-(4-methoxy-1-piperidyl)-1-(2-morpholino-4-pyridyl)pyrazolo[3,4-b]pyridine-6-carboxylic acid



[00668] To a degassed solution of A257 (22 mg, 0.046 mmol, 1.0 equiv) and morpholine (6 µL, 0.069 mmol, 1.5 equiv) in anhydrous THF (1 mL) at RT under nitrogen atmosphere in a sealed vial was added XPhos Pd G1 (CAS 1028206-56-5, 3 mg, 0.0046 mmol, 0.1 equiv) followed by 1 N LiHMDS in THF (138 µL, 0.138 mmol, 3.0 equiv). The reaction mixture was purged with nitrogen, and the vial was sealed. The reaction mixture was stirred at 100 °C for 1.5 h. Additional morpholine (12 µL, 0.138 mmol, 3.0 equiv), 1 N LiHMDS in THF (276 µL, 0.276 mmol, 6.0 equiv) and XPhos Pd G1 (CAS 1028206-56-5, 6 mg, 0.0092 mmol, 0.2 equiv) were added at RT. The reaction mixture was purged again with nitrogen, and the vial was sealed. The reaction mixture was stirred at 100 °C for 1 h. Then the reaction mixture was cooled down and volatiles were removed in vacuo. The resulting residue was taken up in dichloromethane and water and acidified with acetic acid. The two phases were separated, and the aqueous phase was extracted with dichloromethane. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting residue was purified by flash

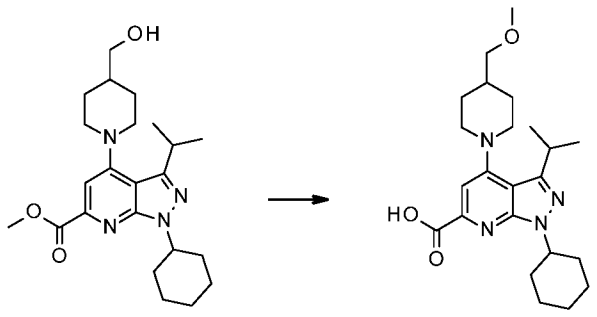
chromatography on silica gel (eluent system dichloromethane/ methanol gradient from 100/0 to 90/10 with 0.1% AcOH) to afford the titled compound.

Method J8: Tandem methylation and saponification



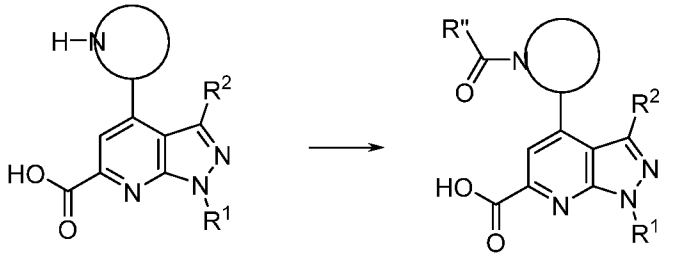
[00669] 60% NaH in mineral oil (6.0 equiv) is added to a solution of an ester/alcohol or a 2-oxo-1,2-dihydropyridin-4-yl/ester (1 equiv) in THF. The reaction mixture is stirred at RT for 5 minutes, and a C_1-C_6 alkyl halide (6.0 equiv) was added. The reaction mixture was stirred at RT for 1-24 hours and then concentrated. The residue was purified by silica gel chromatography to give the ether/carboxylic acid or the 1-methyl-2-oxo-1,2-dihydropyridin-4-yl/carboxylic acid.

Illustrative synthesis of intermediate A162: 1-cyclohexyl-3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]pyrazolo[3,4-b]pyridine-6-carboxylic acid

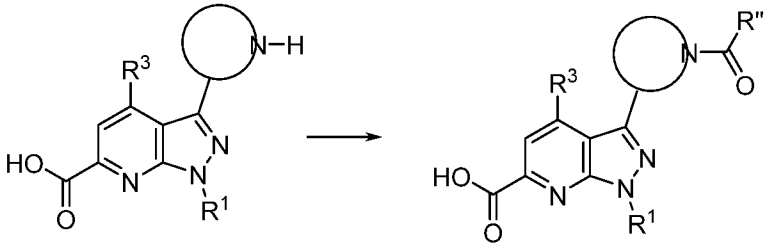


[00670] 60% NaH in mineral oil (24 mg, 0.60 mmol, 6.0 equiv) was added to a solution of E134 (42 mg, 0.10 mmol) in THF (1 mL). The reaction mixture was stirred at RT for 5 minutes, and methyl iodide (0.037 mL, 0.60 mmol, 6.0 equiv) was added. The reaction mixture was stirred at RT for 16 hours and then concentrated. The residue was purified by silica gel chromatography (DCM/MeOH: 100/0 to 90/10) to give the titled compound.

Method J9: amide or carbamate formation from an amine



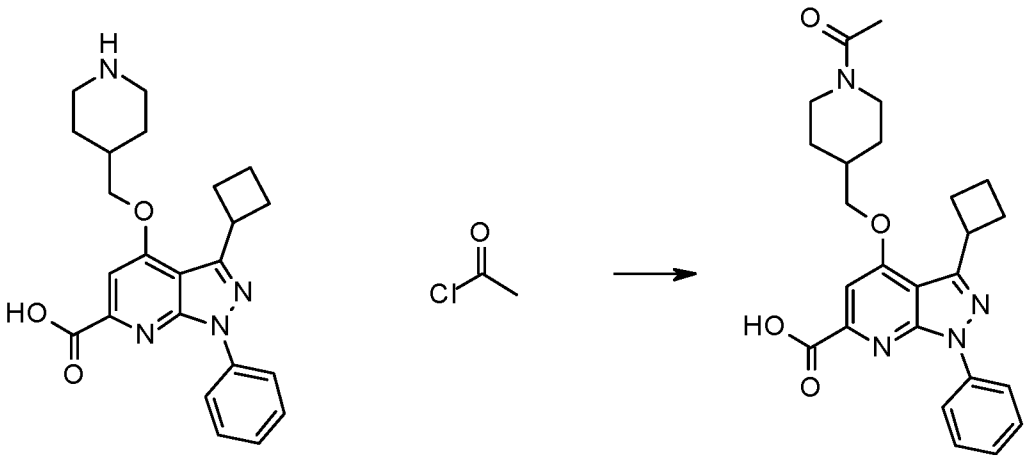
or



R" = C_1-C_6 alkyl or O-C_1-C_6 alkyl

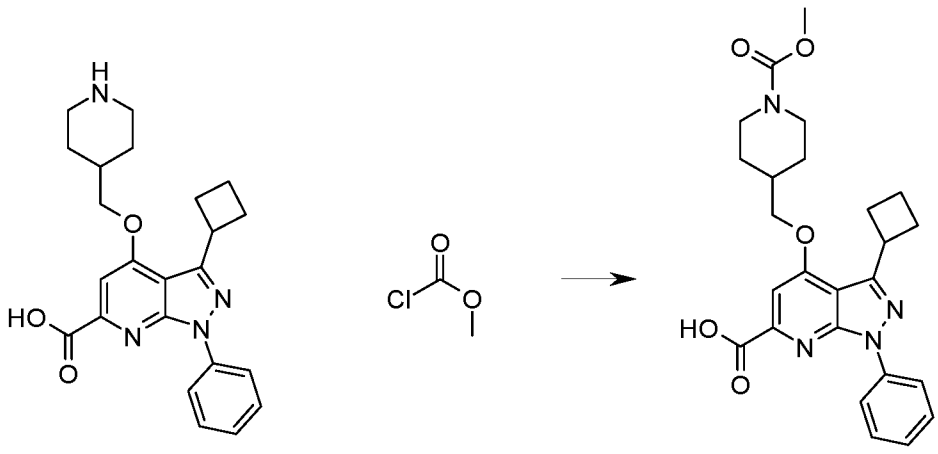
[00671] A heterocyclic amine at either the R^2 or R^3 positions can be reacted with an acid chloride or chloroformate dissolved is solvents such as dichloromethane, tetrahydrofuran or DMF at 0 °C to ambient temperature over 0.5-4 hours in the presence a tertiary amine base or an inorganic carbonate base. The reaction mixture is extractively worked up and/or purified chromatographically either by flash chromatography or by preparative HPLC.

Illustrative synthesis of intermediate A225: 4-[(1-acetyl-4-piperidyl)methoxy]-3-cyclobutyl-1-phenyl-pyrazolo[3,4-b]pyridine-6-carboxylic acid



[00672] To A261 as a trifluoroacetic acid salt (0.43g, 0.83 mmol, 1 equiv) in anhydrous dichloromethane (10 mL) at 0 °C was added triethyl amine (0.69 mL, 4.98 mmol, 6 equiv) followed by acetyl chloride (CAS 75-36-5, 119 µL, 1.66 mmol, 2 equiv). The reaction mixture was stirred at RT for 1 h. The reaction mixture was diluted with dichloromethane and water. The two phases were separated, and the aqueous phase was extracted with dichloromethane. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting residue was purified by flash chromatography on silica gel (eluent system: dichloromethane/methanol gradient from 100/0 to 95/5) to afford the titled compound.

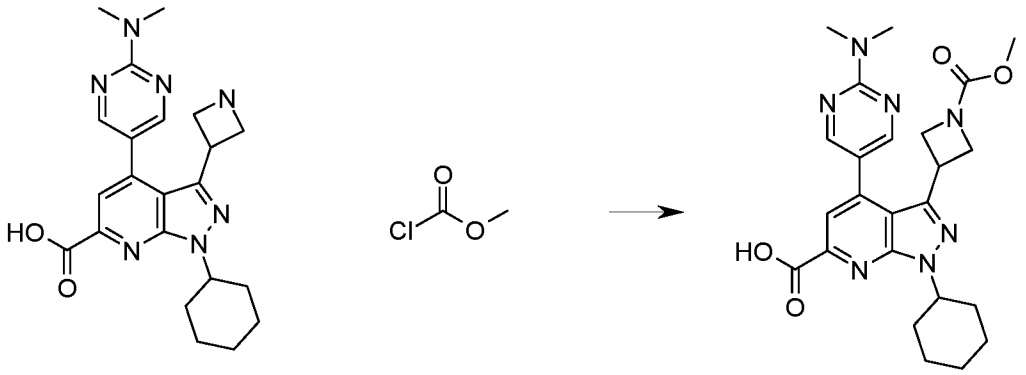
Illustrative synthesis of intermediate A237: 3-cyclobutyl-4-[(1-methoxycarbonyl-4-piperidyl)methoxy]-1-phenyl-pyrazolo[3,4-b]pyridine-6-carboxylic acid



[00673] To A261 as a trifluoroacetic acid salt (0.43g, 0.83 mmol, 1 equiv) in anhydrous dichloromethane (10 mL) at 0 °C was added triethylamine (0.69 mL, 4.98 mmol, 6 equiv)

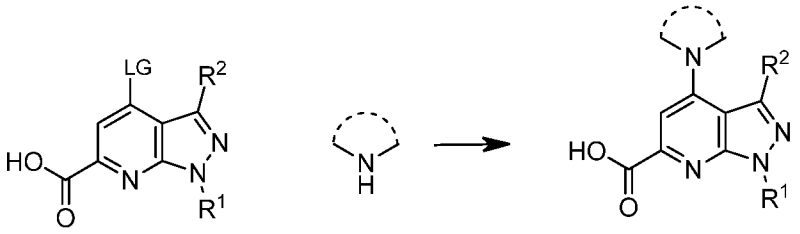
followed by methyl chloroformate (CAS: 79-22-1, 128 µL, 1.66 mmol, 2 equiv). The reaction mixture was stirred at RT for 1 h. The reaction mixture was diluted with dichloromethane and water. The two phases were separated, and the aqueous phase was extracted with dichloromethane. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting residue was taken up in a mixture of THF (1.5 mL), methanol (1.5 mL) and aqueous 2 M sodium hydroxide (0.17 mL) and stirred at RT for 1.5 h. The mixture was concentrated in vacuo. The residue was diluted with ethyl acetate and water and acidified with 1 M HCl (0.34 mL). The two phases were separated, and the aqueous phase was extracted with ethyl acetate. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to afford the titled compound which was used as such.

Illustrative synthesis of intermediate A249: 1-cyclohexyl-4-[2-(dimethylamino)pyrimidin-5-yl]-3-(1-methoxycarbonylazetidin-3-yl)pyrazolo[3,4-b]pyridine-6-carboxylic acid



[00674] Diisopropylethylamine (0.55 mL, 3.12 mmol, 6.0 equiv) and DMAP (13 mg, 0.104 mmol, 0.2 equiv) were added to a solution of A248 (220 mg, 0.52 mmol, 1 equiv) in dichloromethane (2 mL). The mixture was cooled to 0 °C and methyl chloroformate (CAS: 79-22-1, 81 µL, 0.104 mmol, 2.0 equiv) was added. The reaction mixture was warmed up to RT and stirred for 1.5 h. The reaction mixture was partitioned between dichloromethane and water. The two phases were separated, and the aqueous phase was extracted with dichloromethane. The combined organic phase were dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by preparative HPLC to afford the titled compound.

Method J10: Nucleophilic substitution on the central core with amines

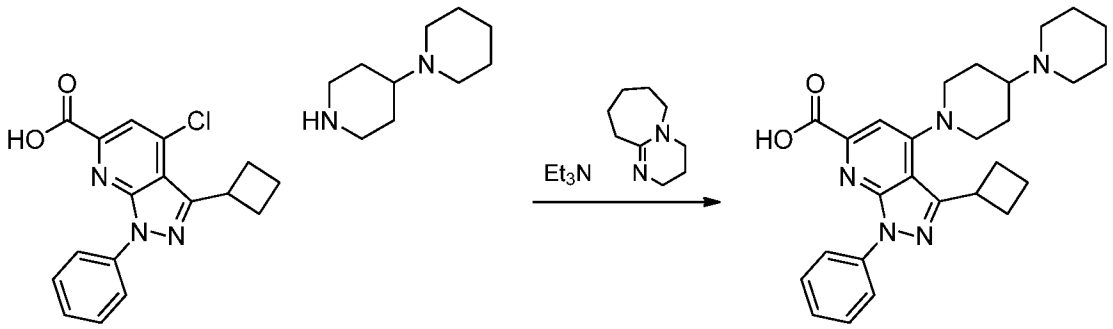


LG = Cl, OTf

[00675] A mixture of the chloride or triflate intermediate HP (1.0 equiv), the amine as free base or hydrochloride salt (from 1 to 10 equiv) and DIPEA (from 1 to 15 equiv) in anhydrous acetonitrile and DMSO or *N*,*N*-dimethylacetamide in a sealed tube or a round bottom flask is heated at a temperature ranging from 50 to 130 °C for 1 h to several days (up to 8 days). The reaction mixture is cooled to RT. The resulting residue is either purified by precipitation or by flash chromatography on silica gel to afford the titled compound or alternatively partitioned between either dichloromethane or ethyl acetate and water. The two phases are then separated, and the aqueous phase is extracted with either ethyl acetate or dichloromethane. The combined organic phases are dried, filtered and concentrated in vacuo, and the resulting crude mixture is either used as such or purified by flash chromatography on silica gel to afford the titled compound.

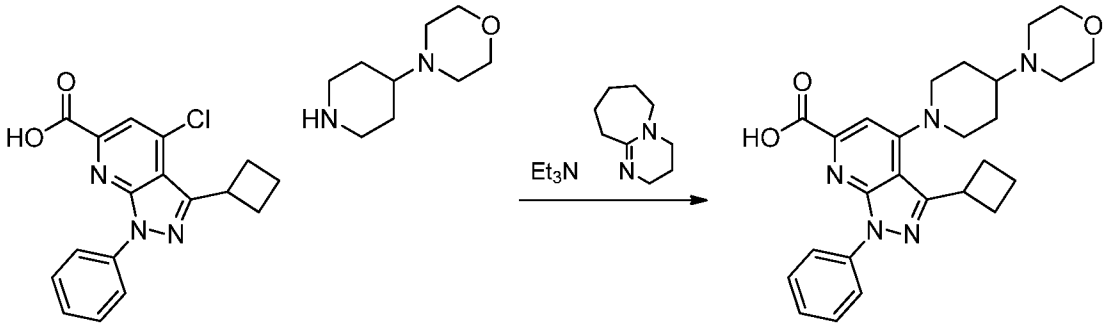
[00676] Alternatively, a mixture of the chloride or triflate intermediate HP (1.0 equiv), the amine as free base or hydrochloride salt (from 1 to 10 equiv) and triethylamine (from 1 to 15 equiv) in *N*,*N*-dimethylacetamide is heated with microwave irradiation at a temperature ranging from 130 to 150 °C for 5 to 20 min. DBU (1 equiv) was added, and the reaction mixture is again heated with microwave irradiation for 1 to 4 hours at 130 to 150 °C Upon cooling, solids are collected and then precipitated from a solvent such as acetonitrile.

Illustrative synthesis of intermediate A081: 3-cyclobutyl-1-phenyl-4-[4-(1-piperidyl)-1-piperidyl]pyrazolo[3,4-b]pyridine-6-carboxylic acid



[00677] A suspension of intermediate HP10 (328 mg, 1.0 mmol), 1,4'-bipiperidine (253 mg, 1.50 mmol) and triethylamine (350 µL, 2.5 mmol) in anhydrous DMA (800 µL) was heated in a Biotage® Initiator microwave synthesizer at 150 °C for fifteen minutes. DBU (180 µL, 1.2 mmol) was added, and the reaction mixture was heated with microwave irradiation at 150 °C for one hour and 45 minutes, brought to room temperature, diluted with water (8 mL) and washed with 1:2 EtOAc/MTBE. The aqueous phase was acidified with 3 M aqueous citric acid (400 µL) to precipitate the product, which was collected by filtration, washed with water and dried under vacuum to give the titled compound (423 mg). ^{1}H NMR (400 MHz, DMSO-d_6, 120 °C) δ ppm 8.32 (d, J = 8.1 Hz, 2H), 7.54-7.48 (m, 2H), 7.32-7.26 (m, 2H), 4.02 (p, J = 8.1 Hz, 1H), 3.63-3.58 (m, 2H), 3.00-2.91 (m, 2H), 2.63-2.57 (m, 4H), 2.56-2.41 (m, 5H), 2.16-1.91 (m, 4H), 1.82-1.69 (m, 2H), 1.60-1.51 (m, 4H), 1.48-1.39 (m, 2H).

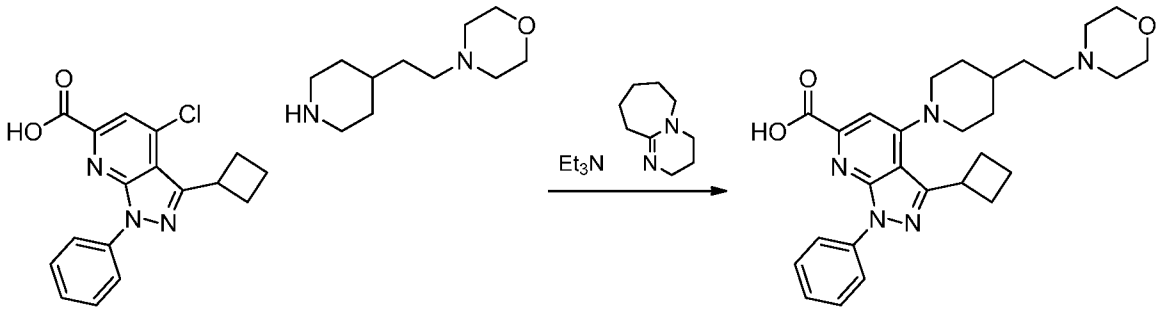
Illustrative synthesis of intermediate A268: 3-cyclobutyl-4-(4-morpholino-1-piperidyl)-1-phenyl-pyrazolo[3,4-b]pyridine-6-carboxylic acid



[00678] A suspension of intermediate HP10 (230 mg, 0.70 mmol), 4-(piperidin-4-yl)morpholine (177 mg, 1.05 mmol) and triethylamine (245 µL, 1.76 mmol) in anhydrous DMA (600 µL) was heated in a Biotage® Initiator microwave synthesizer at 140 °C for five minutes. DBU (105 µL, 0.70 mmol) was added, and the reaction mixture was heated with microwave

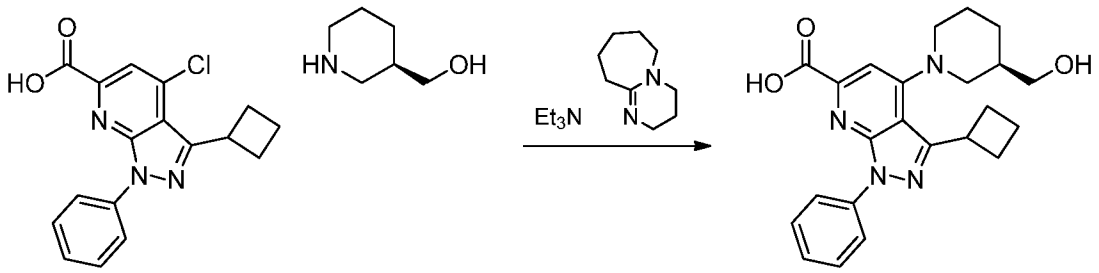
irradiation at 140 °C for three hours, brought to room temperature and filtered through a C18 column (MeOH/H2O). The filtrate was concentrated, and the residual solids were washed with EtOAc, boiled in MeCN and allowed to cool to room temperature. The solid was collected by filtration, rinsed with acetonitrile and dried under vacuum to give the titled compound (305 mg). ^{1}H NMR (400 MHz, DMSO-d_6, 90 °C) δ ppm 8.34-8.30 (m, 2H), 7.54-7.48 (m, 2H), 7.30-7.25 (m, 2H), 4.00 (p, J = 8.1 Hz, 1H), 3.62-3.58 (m, 4H), 3.56-3.53 (m, 2H), 2.97-2.89 (m, 1H), 2.76-2.68 (m, 1H), 2.56-2.51 (m, 4H), 2.45-2.41 (m, 3H), 2.11-1.94 (m, 4H), 1.85-1.77 (m, 1H), 1.74-1.63 (m, 2H), 1.55-1.44 (m, 1H).

Illustrative synthesis of intermediate A270: 3-cyclobutyl-4-[4-(2-morpholinoethyl)-1-piperidyl]-1-phenyl-pyrazolo[3,4-b]pyridine-6-carboxylic acid



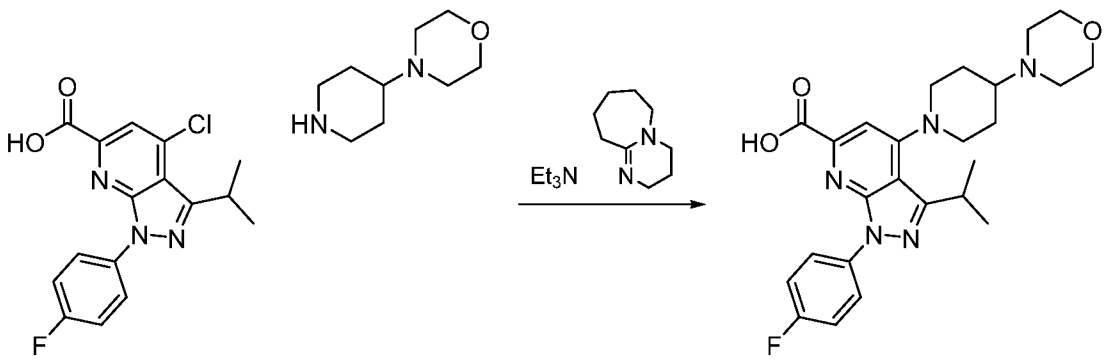
[00679] A suspension of intermediate HP10 (164 mg, 0.50 mmol), 4-(2-(piperidin-4-yl)ethyl)morpholine (149 mg, 0.75 mmol) and triethylamine (175 µL, 1.26 mmol) in anhydrous DMA (400 µL) was heated in a Biotage® Initiator microwave synthesizer at 150 °C for fifteen minutes. DBU (90 µL, 0.60 mmol) was added, and the reaction mixture was heated by microwave irradiation at 150 °C for one hour, brought to room temperature, diluted with water (8 mL) and concentrated. The residue was slurried in acetonitrile and the solids were collected by filtration to give the titled compound (155 mg).

Illustrative synthesis of intermediate A284: 3-cyclobutyl-4-[(3R)-3-(hydroxymethyl)-1-piperidyl]-1-phenyl-pyrazolo[3,4-b]pyridine-6-carboxylic acid



[00680] A suspension of 4-chloro-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (HP10, 164 mg, 0.50 mmol), (*R*)-piperidin-3-ylmethanol (86 mg, 0.75 mmol) and triethylamine (175 µL, 1.26 mmol) in anhydrous DMA (400 µL) was heated in a microwave reactor at 150 °C for fifteen minutes. DBU (90 µL, 0.60 mmol) was added, and the reaction mixture was heated in the reactor at 150 °C for one hour, brought to room temperature, diluted with water (8 mL), concentrated, and purified by preparative HPLC on a Waters® T3 column (30 mm × 100 mm) with a 20 to 100% gradient of acetonitrile in 10 mM aqueous ammonium acetate to give the titled compound (156 mg). ^{1}H NMR (400 MHz, CD_2Cl_2) δ ppm 7.84 (d, J = 8.1 Hz, 2H), 7.21-7.13 (m, 3H), 6.92 (t, J = 7.4 Hz, 1H), 3.81 (tt, J = 8.5, 8.4 Hz, 1H), 3.54-3.46 (m, 1H), 3.43-3.20 (m, 3H), 2.57-2.24 (m, 6H), 2.04-1.88 (m, 2H), 1.84-1.71 (m, 1H), 1.63-1.49 (m, 3H), 0.95-0.79 (m, 1H).

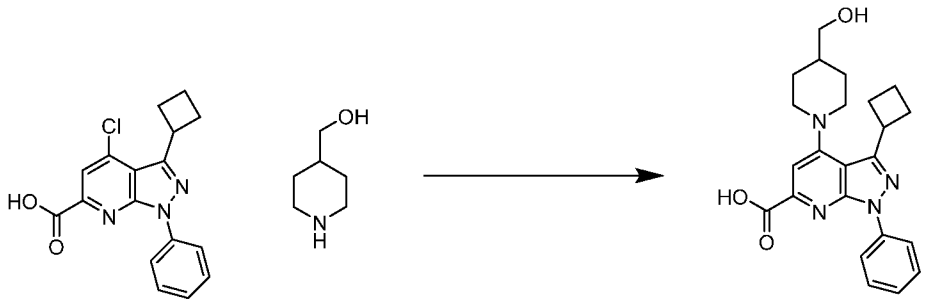
Illustrative synthesis of intermediate A408: 1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-3-(propan-2-yl)-1H-pyrazolo[3,4-b]pyridine-6-carboxylic acid



[00681] A suspension of the 4-chloro-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (267 mg, 0.80 mmol, HP11), 4-morpholinopiperidine (204 mg, 1.2 mmol) and triethylamine (280 µL, 2.0 mmol) in anhydrous DMA (700 µL) was heated in a microwave reactor at 150 °C for fifteen minutes. DBU (145 µL, 0.96 mmol) was added, and the reaction mixture was heated at 150 °C two hours, brought to room temperature, diluted with water (7 mL) and washed twice with 1:2 EtOAc/MTBE. The aqueous phase was acidified with

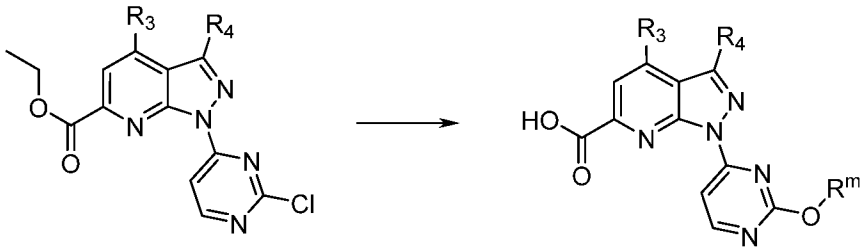
aqueous citric acid to pH 5, and the solids were collected by filtration, washed with water and dried under vacuum to give the titled compound.

Illustrative synthesis of compound A413: 3-cyclobutyl-4-[4-(hydroxymethyl)piperidin-1-yl]-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxylic acid



[00682] To a solution of HP10 (0.502 g, 1.532 mmol) and 4-piperidinemethanol (0.441 g, 3.83 mmol) in *N*,*N*-dimethylacetamide (DMA, 1.5 mL) was added diisopropylethylamine (1.5 mL, 8.59 mmol), and the reaction mixture was then stirred at 150 °C for 12 hours. The reaction mixture was then partitioned between dichloromethane and 1 N HCl. The organic fraction was separated, dried over anhydrous sodium sulfate, filtered, and concentrated under vacuum. The residue was purified on silica gel, eluting with a gradient of 0-5% MeOH/DCM to give the titled compound. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.41 (qd, J = 12.2, 3.7 Hz, 2H), 1.60 (dtdd, J = 13.2, 10.0, 6.2, 3.6 Hz, 1H), 1.83 (dd, J = 13.3, 3.4 Hz, 2H), 1.87 – 2.12 (m, 3H), 2.36 (dtd, J = 11.8, 8.5, 3.1 Hz, 2H), 2.51 (dd, J = 9.3, 2.3 Hz, 1H), 2.76 – 2.96 (m, 2H), 3.54 (dd, J = 9.4, 6.2 Hz, 2H), 3.94 (p, J = 8.4 Hz, 1H), 4.55 (s, 1H), 7.24 – 7.33 (m, 2H), 7.47 – 7.58 (m, 2H), 8.30 (d, J = 8.0 Hz, 2H).

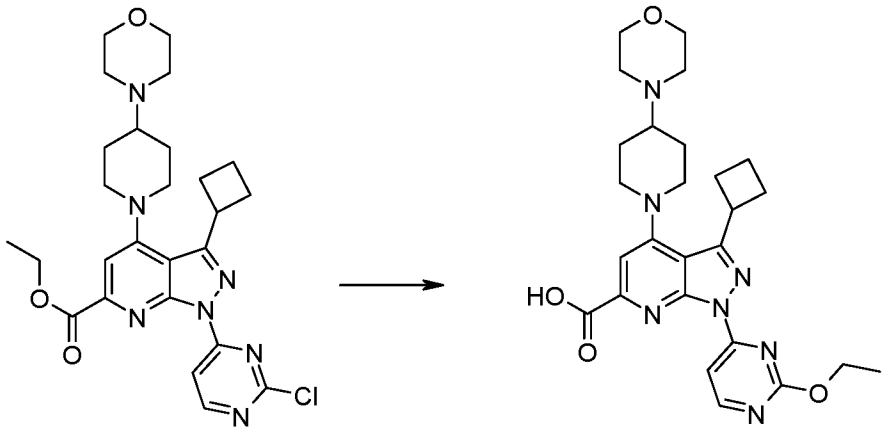
Method J11: Tandem nucleophilic substitution/saponification



R^m: isopropyl, ethyl

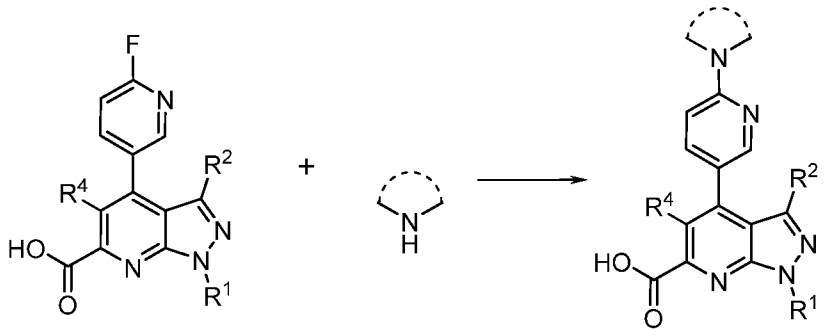
[00683] The intermediate ester (1 equiv) is suspended in a mixture of appropriate alcohol for the nucleophilic substitution and THF. 1 N NaOH (from 17 to 19 equiv) is added, and the reaction mixture is stirred at RT or 50 °C until full conversion is observed. 1 N HCl (2 equiv) and a phosphate buffer solution (pH 6.2) are added. The mixture is concentrated under reduced pressure, and the crude residue is partitioned between water and dichloromethane. The organic phase is dried over sodium sulfate, filtered and concentrated under reduced pressure to give the titled compound.

Illustrative synthesis of A343: 3-cyclobutyl-1-(2-ethoxypyrimidin-4-yl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1H-pyrazolo[3,4-b]pyridine-6-carboxylic acid



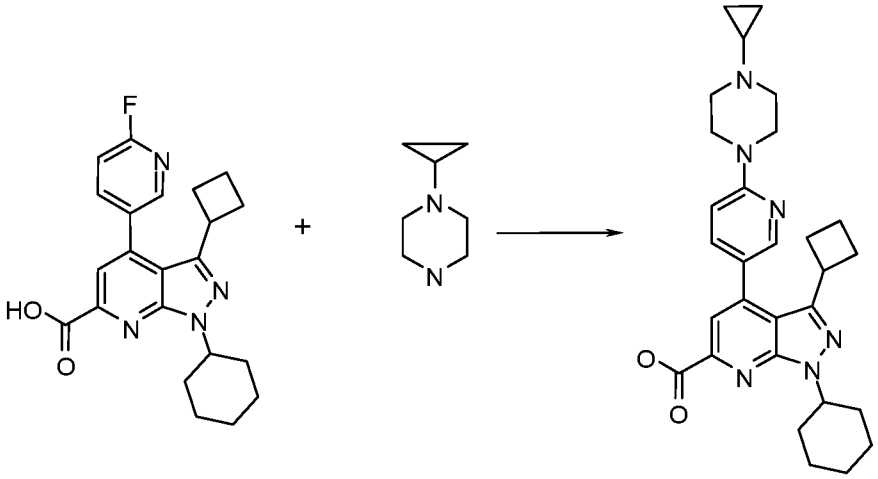
[00684] The intermediate ester E422 (30 mg, 57 µmol) was suspended in a mixture of ethanol (8 mL) and THF (3 mL). 1 N NaOH (1 mL, 1 mmol) was added, and the reaction mixture was stirred at RT for 2 hours. 1N HCl (1 mL, 1 mmol) and a phosphate buffer solution (pH 6.2, 5 mL) were added. The mixture was concentrated under reduced pressure, and the crude residue was partitioned between water and dichloromethane. The organic phase was dried over sodium sulfate, filtered and concentrated under reduced pressure to give the titled compound, A343.

Method J12: S_NAr on fluoropyridine



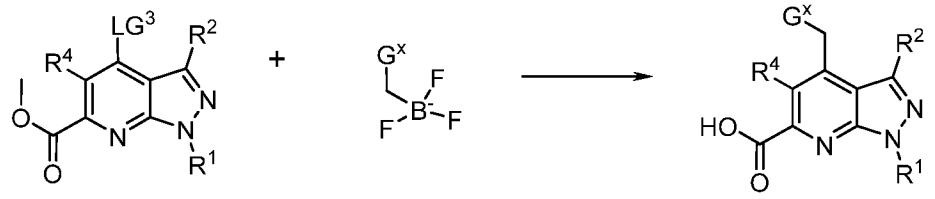
[00685] The (6-fluoro-pyridin-3-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (1 eq) is heated together with the amine (1.05 eq) and DIPEA (1.25 eq) in NMP at 100 °C for 18 hours. Mixture is diluted with EtOAc and water. Isolation of the organic layer and subsequent concentration yields the desired product.

Illustrative synthesis of compound A405: 3-Cyclobutyl-1-cyclohexyl-4-[6-(4-cyclopropyl-piperazin-1-yl)-pyridin-3-yl]-1H-pyrazolo[3,4-b]pyridine-6-carboxylic acid



[00686] 3-Cyclobutyl-1-cyclohexyl-4-(6-fluoro-pyridin-3-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (200 mg, 0.51 mmol) was heated together with 1-cyclopropylpiperazine ([20327-23-5], 64 µL, 0.53 mmol) and DIPEA (110 µL, 0.64 mmol) in NMP (2 mL) at 100 °C for 18 hours. The mixture was diluted with EtOAc and water. Isolation of the organic layer and subsequent concentration yielded the titled compound.

Method J13: Suzuki with alkyl-BF_3 salts



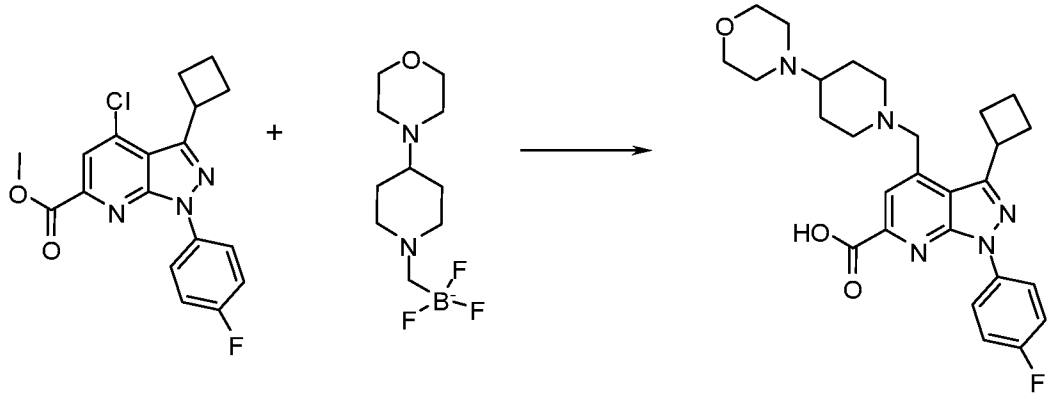
LG^3 is a leaving group suitable for the coupling reaction

G^x is $-G^{3B}$ or $-G^{3B}-L^1-G^{3C}$

[00687] The aryl halide (1 eq) is mixed together with the alkyl-BF3 salt (1.5 eq), $Pd(dppf)Cl_2$•DCM (CAS 95464-05-4, 0.05 eq) and Cs_2CO_3 (3 eq) in a mixture of THF/H_2O (10/1). The mixture is put under N_2 atmosphere and heated at 80 °C overnight.

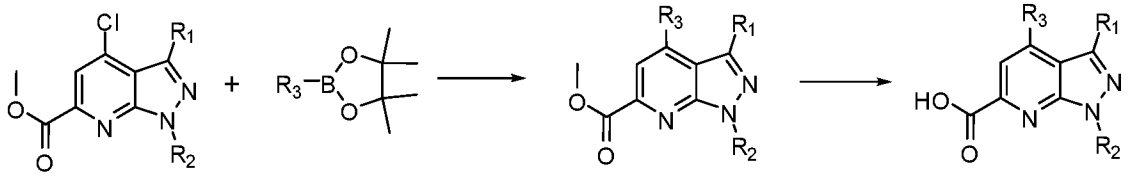
[00688] If the method is performed on an ester, the ester can be subsequently hydrolyzed to the acid by the addition of LiOH (2 eq) and heating at 50 °C. The titled compound is isolated by acidifying with citric acid till pH = 6 and extraction with EtOAc. Concentration, possibly followed by chromatographic purification, gives the titled compound.

Illustrative synthesis of compound A361: 3-Cyclobutyl-1-(4-fluoro-phenyl)-4-(4-morpholin-4-yl-piperidin-1-ylmethyl)-1H-pyrazolo[3,4-b]pyridine-6-carboxylic acid



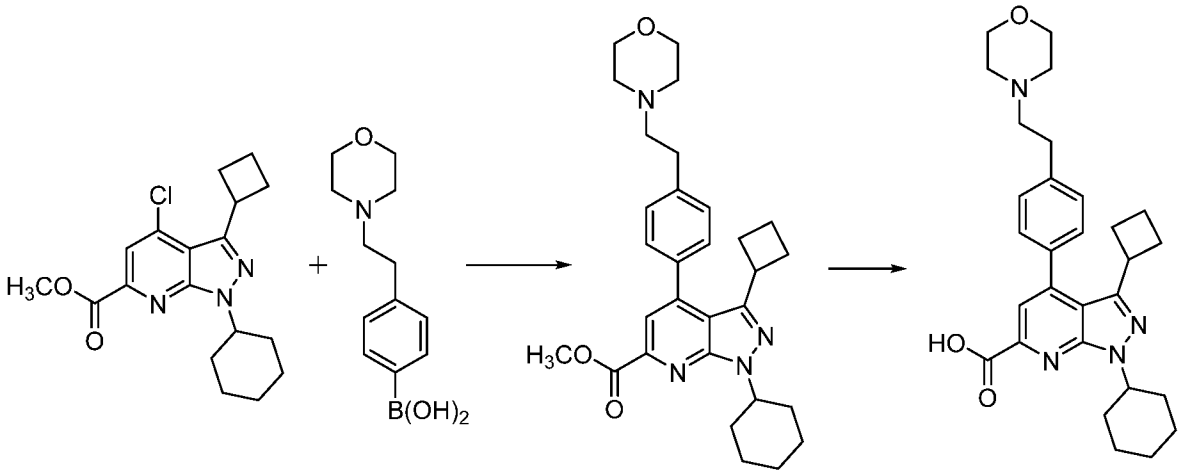
[00689] HP19 (352 mg, 0.98 mmol) was mixed together with the potassium trifluorido{[4-(morpholin-4-yl)piperidin-1-yl]methyl}borate (426 mg, 1.47 mmol), $Pd(dppf)Cl_2$•DCM (CAS 95464-05-4, 40 mg, 0.05 mmol) and Cs_2CO_3 (959 mg, 2.94 mmol) in a mixture of THF/H_2O (10/1, 5 mL). The mixture was put under a N_2 atmosphere and heated at 80 °C overnight. Next, LiOH (82 mg, 2 mmol) was added, and the mixture was heated at 50 °C. The titled compound was isolated by acidifying with citric acid till pH = 6 and extraction with EtOAc. Concentration, followed by automated preparative chromatographic purification, gave the titled compound.

Method J14: Suzuki and subsequent hydrolysis



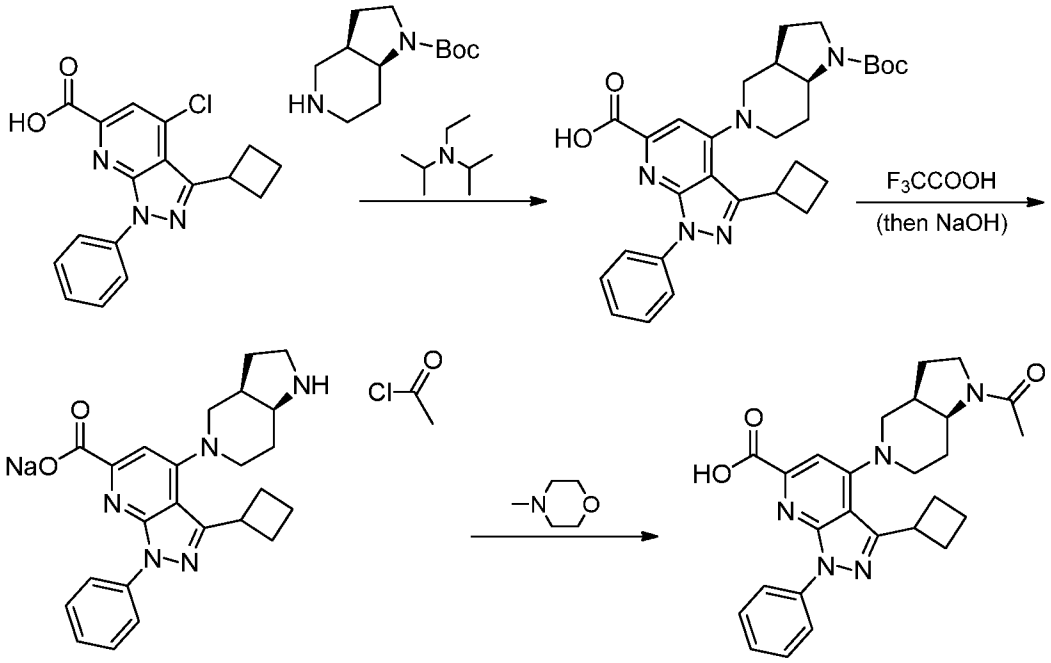
[00690] The arylchloride (1 eq) is mixed with the boronic ester (or acid) (1.5 eq), $Pd(dppf)Cl_2$•DCM (CAS 95464-05-4, 0.1 eq) and DIPEA (3 eq) in a mixture of water/dioxane (1/2). The resulting mixture is stirred at 120 °C for 18 hours. Next, LiOH (2 eq) is added, and the mixture is heated at 40 °C. After acidifying with 2 M HCl solution, extraction with EtOAc gives an organic phase that is concentrated to give the titled compound.

Illustrative synthesis of compound A365: 3-cyclobutyl-1-cyclohexyl-4-{4-[2-(morpholin-4-yl)ethyl]phenyl}-1H-pyrazolo[3,4-b]pyridine-6-carboxylic acid



[00691] Intermediate HP25 (140 mg, 0.40 mmol), 4-(2-morpholinoethyl)phenylboronic acid (142 mg, 0.60 mmol, CAS#1150114-55-8), $Pd(dppf)_2Cl_2$ (33 mg, 0.04 mmol) and DIPEA (211 µL, 1.20 mmol) were heated at 120 °C in a mixture of water and dioxane (3 mL, 1:2 water/dioxane). After overnight stirring, LiOH (34 mg, 0.81 mmol) was added, and the resulting mixture was stirred at 40 °C until the hydrolysis was finished. Next, the mixture was diluted with EtOAc and water. After separation, the aqueous phase was acidified with 2 N HCl and subsequently extracted with DCM. The resulting organic phase was dried and concentrated to give the titled compound.

Synthesis of A271: 4-[(3aR,7aS)-1-acetyl-3,3a,4,6,7,7a-hexahydro-2H-pyrrolo[3,2-c]pyridin-5-yl]-3-cyclobutyl-1-phenyl-pyrazolo[3,4-b]pyridine-6-carboxylic acid



[00692] *Step 1: rac-4-[(3aR,7aS)-1-(tert-butoxycarbonyl)octahydro-5H-pyrrolo[3,2-c]pyridin-5-yl]-3-cyclobutyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxylic acid*

[00693] Intermediate HP10 (164 mg, 0.50 mmol), the *tert*-butyl *rac*-(3a*R*,7a*S*)-octahydro-1*H*-pyrrolo[3,2-*c*]pyridine-1-carboxylate (181 mg, 0.80 mmol, CAS#848410-13-9) and diisopropylethylamine (175 µL, 1.0 mmol) were heated in DMSO (350 µL) at 120 °C for a day, brought to room temperature, and partitioned between EtOAc and 2:1 water/brine (600 µL). The aqueous phase was separated and extracted thrice with EtOAc, and the combined organic phases were acidified with TFA, concentrated and chromatographed on silica (0.1% TFA in 1:1 EtOAc/heptane) to give the titled compound (274 mg). ^{1}H NMR (501 MHz, methanol-d_4) δ ppm 1.50 (s, 9H), 1.94 2.27 (m, 6H), 2.42-2.51 (m, 2H), 2.52-2.66 (m, 3H), 2.95-3.06 (m, 1H), 3.37-3.58 (m, 5H), 3.94-4.00 (m, 1H), 4.02-4.07 (m, 1H), 7.31-7.35 (m, 1H), 7.44 (s, 1H), 7.50-7.55 (m, 2H), 8.24-8.28 (m, 2H).

[00694] *Step 2: sodium rac-3-cyclobutyl-4-[(3aR,7aS)-octahydro-5H-pyrrolo[3,2-c]pyridin-5-yl]-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxylate*

[00695] *rac*-4-[(3a*R*,7a*S*)-1-(*tert*-Butoxycarbonyl)octahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl]-3-cyclobutyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (1.00 g, <1.9 mmol) was dissolved into anhydrous CH_2Cl_2 (8.0 mL), treated with TFA (2.0 mL), stirred at room temperature for two hours and then concentrated. The residue was redissolved into CH_2Cl_2, treated with aqueous K_2HPO_4 and basified to pH 11+ with aqueous NaOH. Brine was added, and the mixture was extracted with 10% MeOH/CH_2Cl_2. The separated organic phase was dried (Na_2SO_4), passed through a short column of Na_2SO_4 and concentrated to give the titled compound (452 mg). ^{1}H NMR (500 MHz, methanol-d_4) δ ppm 1.69-1.77 (m, 1H), 1.98-2.21 (m, 5H), 2.40-2.66 (m, 6H), 2.94-3.01 (m, 2H), 3.15-3.3 (m, 3H), 3.32-3.36 (m, 1H), 4.07-4.15 (m, 1H), 7.24-7.28 (m, 1H), 7.38 (s, 1H), 7.47-7.51 (m, 2H), 8.35-8.38 (m, 2H); MS (ESI) *m/z* 418 $(M+H)^+$.

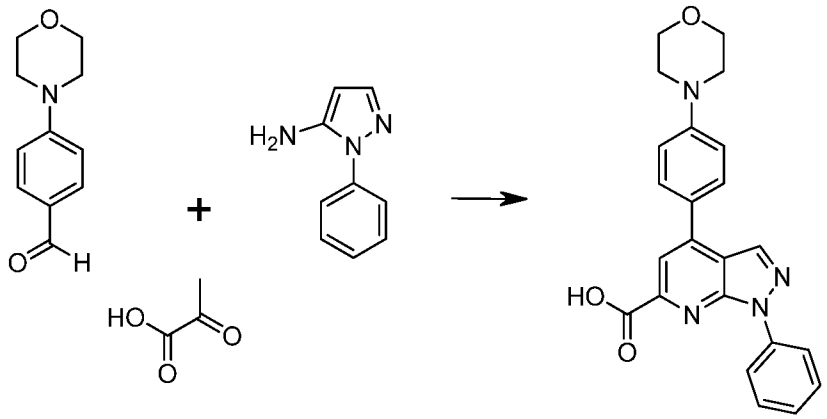
[00696] *Step 3: 4-[(3aR,7aS)-1-acetyl-3,3a,4,6,7,7a-hexahydro-2H-pyrrolo[3,2-c]pyridin-5-yl]-3-cyclobutyl-1-phenyl-pyrazolo[3,4-b]pyridine-6-carboxylic acid*

[00697] Sodium *rac*-3-cyclobutyl-4-[(3a*R*,7a*S*)-octahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylate (209 mg, 0.50 mmol) and *N*-methylmorpholine (220 μL, 2.0 mmol) were suspended in DMF (2.5 mL) and chilled with a water ice bath. A solution of acetyl chloride (50 μL, 0.70 mmol) in dichloromethane (500 μL) was added dropwise, and the mixture was stirred for two minutes before the bath was removed. The cloudy solution was stirred another thirty minutes at room temperature before being diluted with EtOAc and placed directly on silica for chromatography (EtOAc, then 0 to 20% MeOH/MeCN, then 0.1% TFA/19.9% MeOH/80% MeCN) to give *rac*-4-[(3a*R*,7a*S*)-1-acetyloctahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl]-3-cyclobutyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (236 mg).

[00698] The racemate was then subjected to preparative supercritical fluid chromatography set to maintain a maximum back pressure of 100 MPa using a Chiralcel® OJ-H (21 x 250 mm) column with the sample at a concentration of 10 mg/mL in methanol using 35% methanol in CO_2 at a flow rate of 45 mL/minute to provide both enantiomers separately. The first enantiomer eluted (retention time = 5.4 minutes), and the second enantiomer eluted (retention time = 7.4 minutes) as the titled compound (stereochemistry arbitrarily assigned). ^{1}H NMR (400 MHz, DMSO-d_6, 120 °C) δ ppm 1.98 (s, 3H), 1.88-2.22 (m, 6H), 2.40-2.59 (m, 4H), 2.98-3.07 (m, 1H),

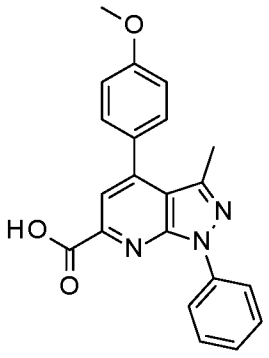
3.15-3.19 (m, 1H), 3.31-3.61 (m, 4H), 3.78-3.83 (m, 1H), 3.99-4.13 (m, 2H), 7.27-7.32 (m, 1H), 7.34 (s, 1H), 7.49-7.55 (m, 2H), 8.29-8.35 (m, 2H).

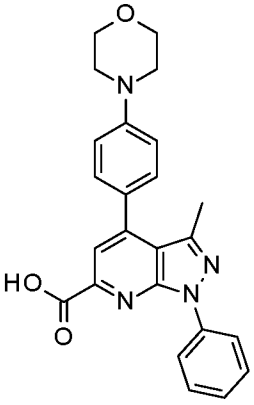
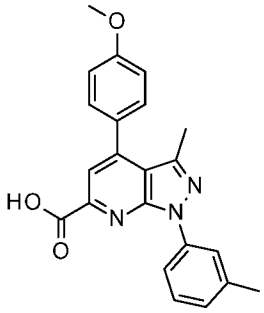
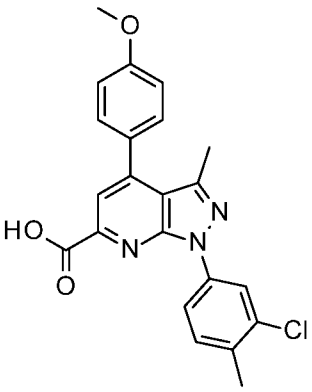
Synthesis of A222: 4-(4-morpholinophenyl)-1-phenyl-pyrazolo[3,4-b]pyridine-6-carboxylic acid

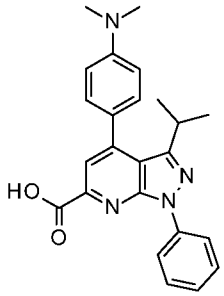
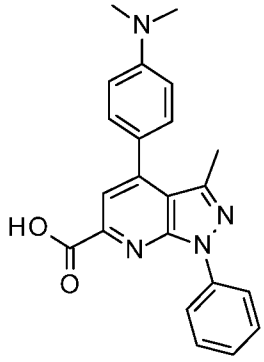
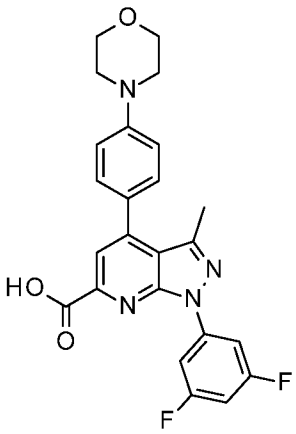


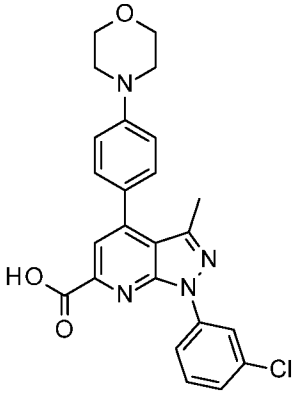
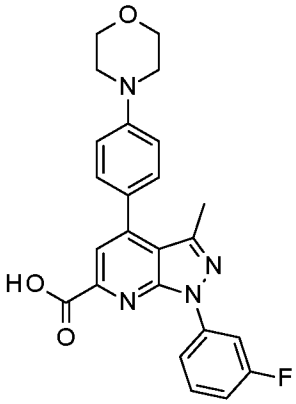
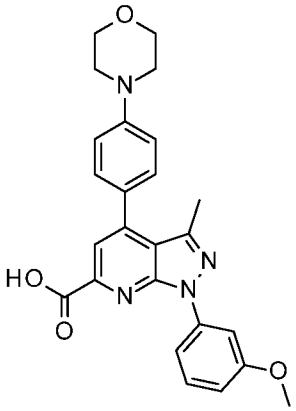
[00699] 4-(4-Morpholinyl)benzaldehyde (CAS 1204-86-0, 241 mg, 1.26 mmol, 1 equiv), pyruvic acid (CAS 127-17-3, 88 µL, 1.26 mmol, 1 equiv) and 5-amino-1-phenylpyrazole (CAS 826-85-7, 200 mg, 1.26 mmol, 1 equiv) were combined in a sealed tube. Acetic acid (5 mL) was added, and the vial was sealed. The reaction mixture was heated under microwave irradiation at 160 °C for 20 min. The reaction mixture was cooled down and concentrated in vacuo. The resulting residue was purified by preparative HPLC to afford the tiled compound.

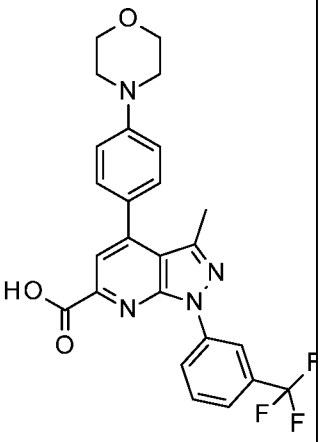
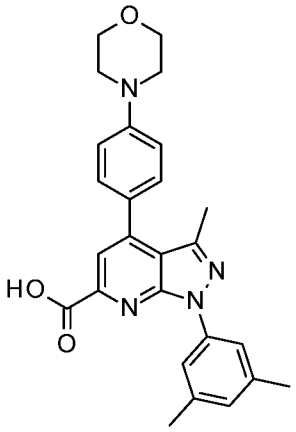
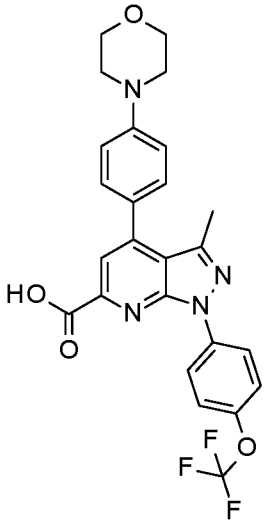
Table XIII. List of acids

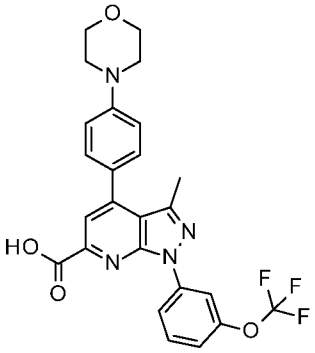
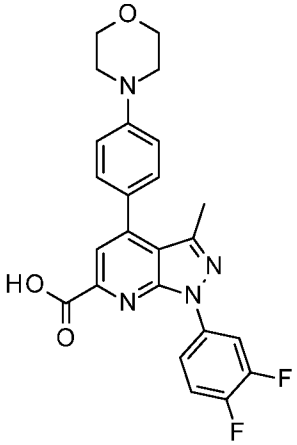
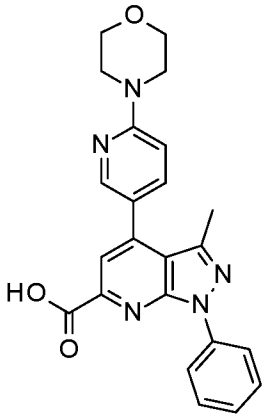
Int.	Structure	Name	SM	method	MW	Mes
A001		4-(4-methoxyphenyl)-3-methyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	/	926282-55-5	/	/

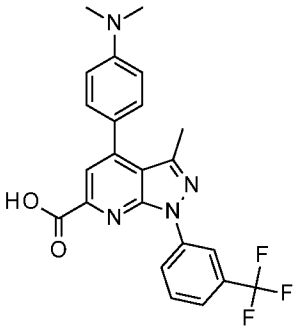
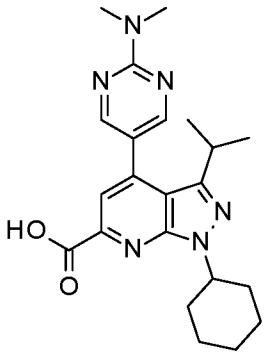
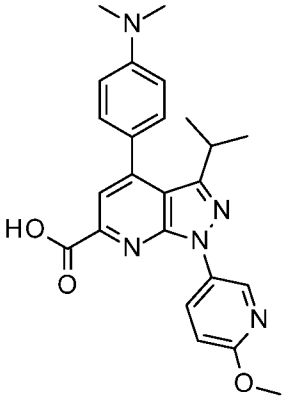
Int.	Structure	Name	SM	method	MW	Mes
A002		3-methyl-4-(4-morpholinophenyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP01, 1131-18-6	J2 Specific example	414	415
A003		4-(4-methoxyphenyl)-3-methyl-1-(*m*-tolyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP06, 92721-83-0	J2	373	374
A004		1-(3-chloro-4-methyl-phenyl)-4-(4-methoxyphenyl)-3-methyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP06, 866472-29-9	J2	407	408

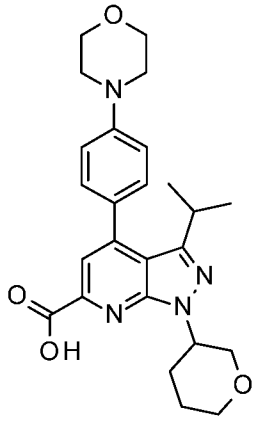
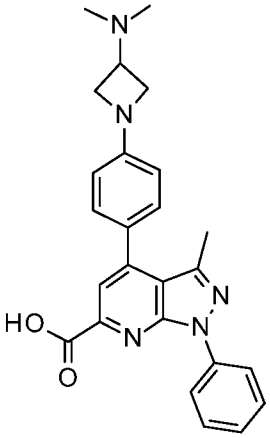
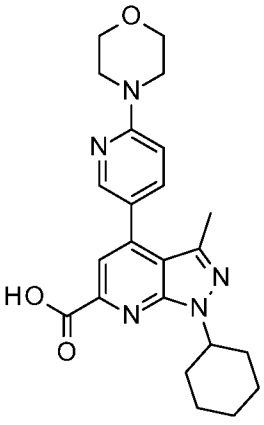
Int.	Structure	Name	SM	method	MW	Mes
A005		4-[4-(dimethylamino)phenyl]-3-isopropyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP02, AMP04	J2	400	401
A006		4-(4-dimethylaminophenyl)-3-methyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E006	J1	372	373
A007		1-(3,5-difluorophenyl)-3-methyl-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP01, 1232796-65-4	J2	450	451

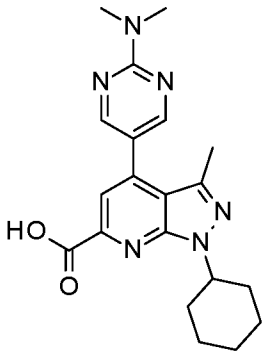
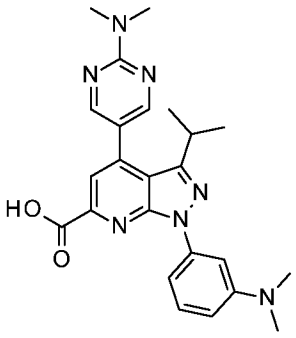
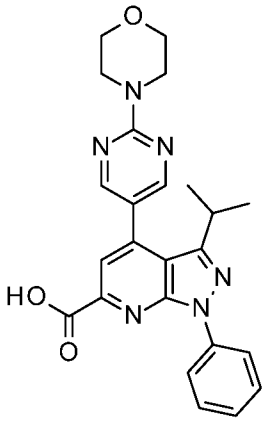
Int.	Structure	Name	SM	method	MW	Mes
A008		1-(3-chlorophenyl)-3-methyl-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP01, 40401-41-0	J2	448	449
A009		1-(3-fluorophenyl)-3-methyl-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP01, 105438-45-7	J2	432	433
A010		1-(3-methoxyphenyl)-3-methyl-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP01, 92721-94-3	J2	444	445

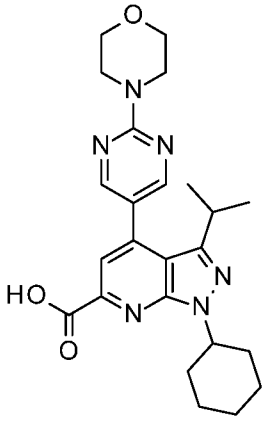
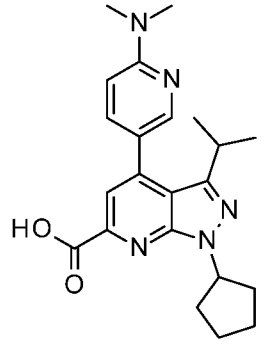
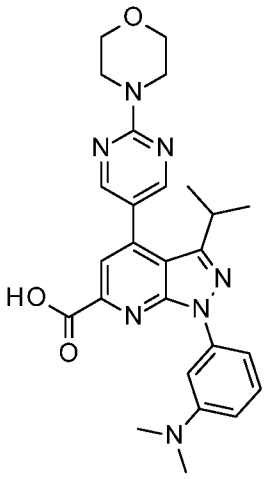
Int.	Structure	Name	SM	method	MW	Mes
A011		3-methyl-4-(4-morpholinophenyl)-1-[3-(trifluoromethyl)phenyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP01, 345-07-3	J2	482	483
A012		1-(3,5-dimethylphenyl)-3-methyl-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP01, 890010-89-6	J2	442	443
A013		3-methyl-4-(4-morpholinophenyl)-1-[4-(trifluoromethoxy)phenyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP01, 497141-59-0	J2	414	415

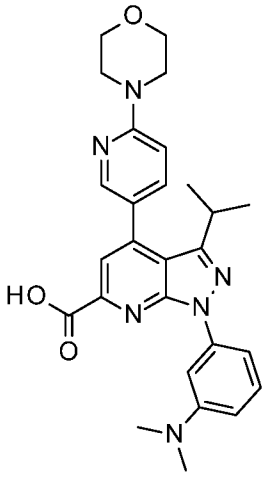
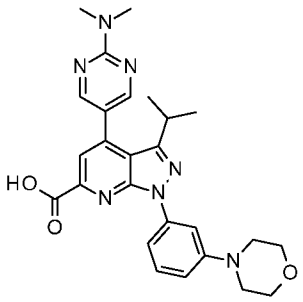
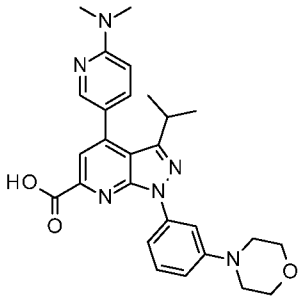
Int.	Structure	Name	SM	method	MW	Mes
A014		3-methyl-4-(4-morpholinophenyl)-1-[3-(trifluoromethoxy)phenyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP01, AMP01	J2	498	499
A015		1-(3,4-difluorophenyl)-3-methyl-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP01, AMP02	J2	450	451
A016		3-methyl-4-(6-morpholino-3-pyridyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E009	J1	415	416

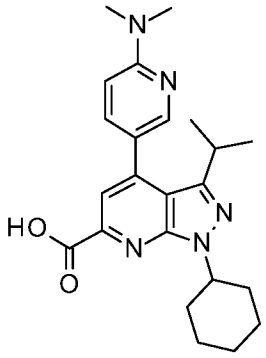
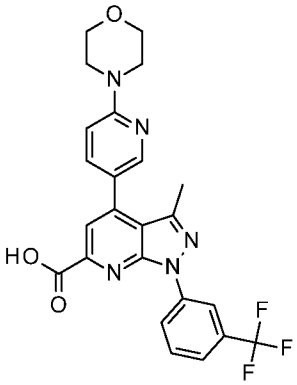
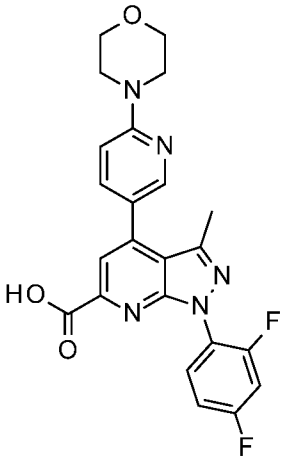
Int.	Structure	Name	SM	method	MW	Mes
A017		4-(4-dimethylaminophenyl)-3-methyl-1-[3-(trifluoromethyl)phenyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP02, 345-07-3	J2	440	441
A018		cyclohexyl-4-[2-(dimethylamino)pyrimidin-5-yl]-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP03, AMP23	J2	408	409
A019		4-[4-(dimethylamino)phenyl]-3-isopropyl-1-(6-methoxy-3-pyridyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP02, AMP16	J2	431	432

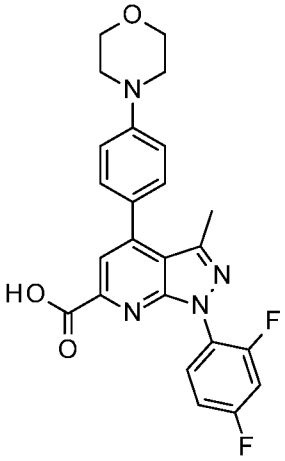
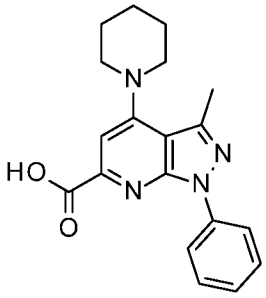
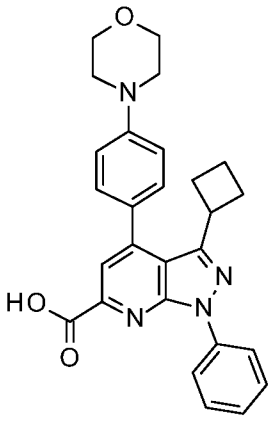
Int.	Structure	Name	SM	method	MW	Mes
A020		3-isopropyl-4-(4-morpholinophenyl)-1-tetrahydropyran-3-yl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP01, AMP25	J2	450	451
A021		4-[4-[3-(dimethylamino)azetidin-1-yl]phenyl]-3-methyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E011	J1	427	428
A022		1-cyclohexyl-3-methyl-4-(6-morpholino-3-pyridyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP05, 56547-82-1	J2	421	422

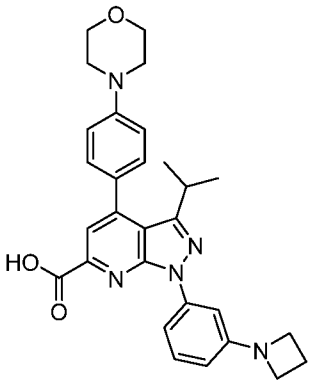
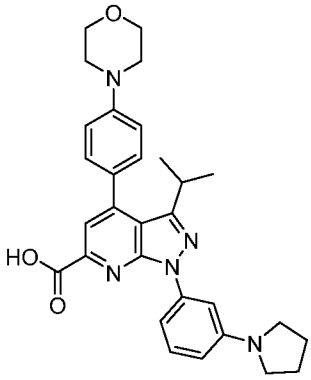
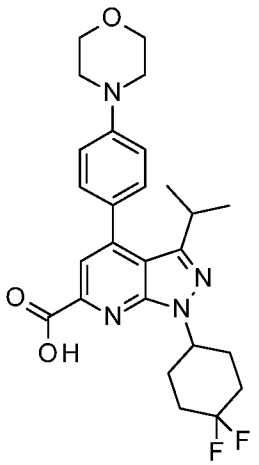
Int.	Structure	Name	SM	method	MW	Mes
A023		1-cyclohexyl-4-[2-(dimethylamino)pyrimidin-5-yl]-3-methyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP03, 56547-82-1	J2	380	381
A024		1-[3-(dimethylamino)phenyl]-4-[2-(dimethylamino)pyrimidin-5-yl]-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP03, AMP06	J2	445	446
A025		3-isopropyl-4-(2-morpholinopyrimidin-5-yl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP04, AMP04	J2	444	445

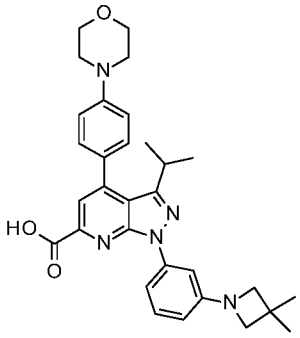
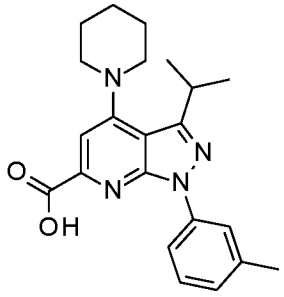
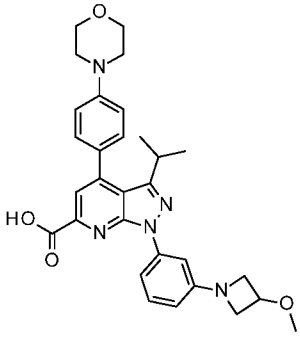
Int.	Structure	Name	SM	method	MW	Mes
A026		3-isopropyl-4-(2-morpholinopyrimidin-5-yl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E003	J1	450	451
A027		1-cyclopentyl-4-[6-(dimethylamino)-3-pyridyl]-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP21, AMP26	J2	393	394
A028		1-[3-(dimethylamino)phenyl]-3-isopropyl-4-(2-morpholinopyrimidin-5-yl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E016	J1	487	488

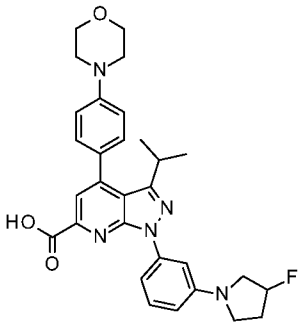
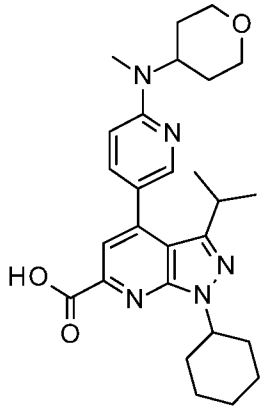
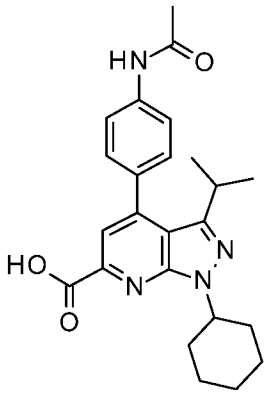
Int.	Structure	Name	SM	method	MW	Mes
A029		1-[3-(dimethylamino)phenyl]-3-isopropyl-4-(6-morpholino-3-pyridyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E015	J1	486	487
A030		4-[2-(dimethylamino)pyrimidin-5-yl]-3-isopropyl-1-(3-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP03, AMP10	J2	487	488
A031		4-[6-(dimethylamino)-3-pyridyl]-3-isopropyl-1-(3-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP21, AMP10	J2	486	487

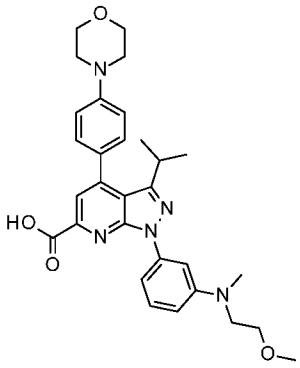
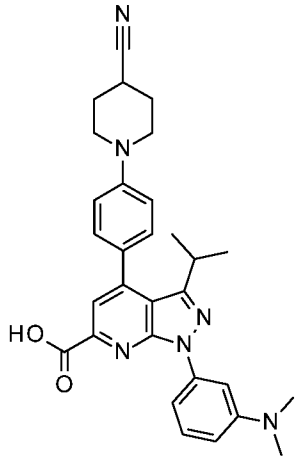
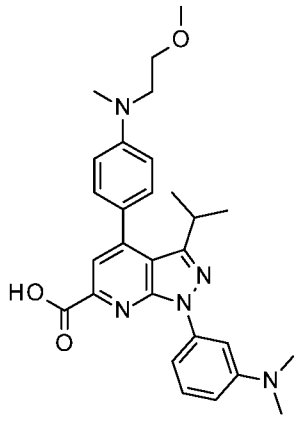
Int.	Structure	Name	SM	method	MW	Mes
A032		1-cyclohexyl-4-[6-(dimethylamino)-3-pyridyl]-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP21, AMP23	J2	407	408
A033		3-methyl-4-(6-morpholino-3-pyridyl)-1-[3-(trifluoromethyl)phenyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP05, 345-07-3	J2	483	484
A034		1-(2,4-difluorophenyl)-3-methyl-4-(6-morpholino-3-pyridyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP05, 380569-79-9	J2	451	452

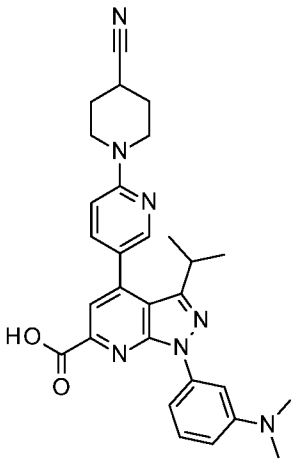
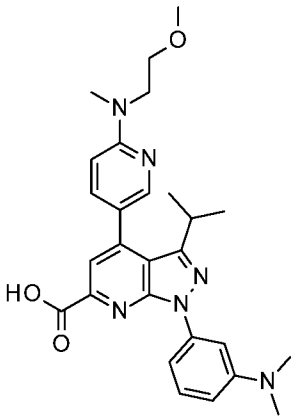
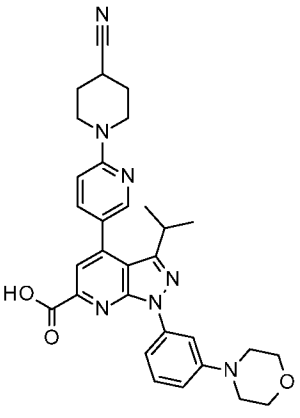
Int.	Structure	Name	SM	method	MW	Mes
A035		1-(2,4-difluorophenyl)-3-methyl-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP01, 380569-79-9	J2	450	451
A036		3-methyl-1-phenyl-4-(1-piperidyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E004	J1	336	337
A037		3-cyclobutyl-4-(4-morpholinophenyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP01, AMP29	J2	454	455

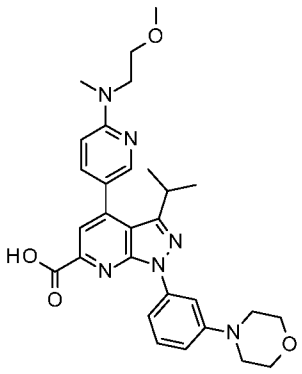
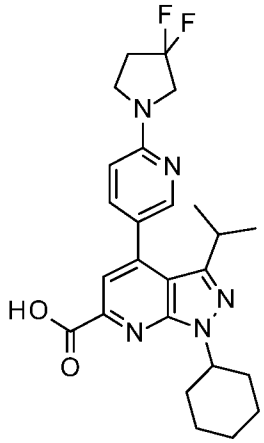
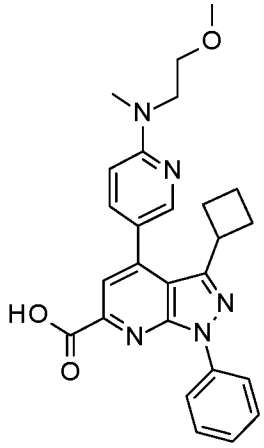
Int.	Structure	Name	SM	method	MW	Mes
A038		1-[3-(azetidin-1-yl)phenyl]-3-isopropyl-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E002	J1	497	498
A039		3-isopropyl-4-(4-morpholinophenyl)-1-(3-pyrrolidin-1-ylphenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E005	J1	511	512
A040		1-(4,4-difluorocyclohexyl)-3-isopropyl-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP01, AMP24	J2	484	485

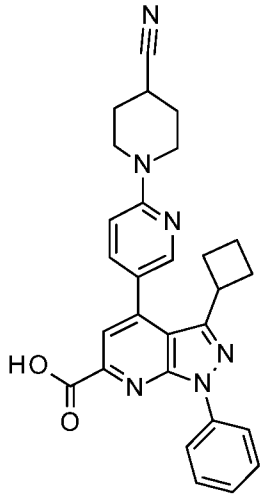
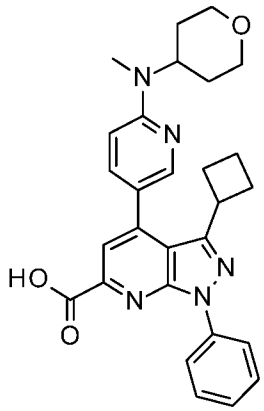
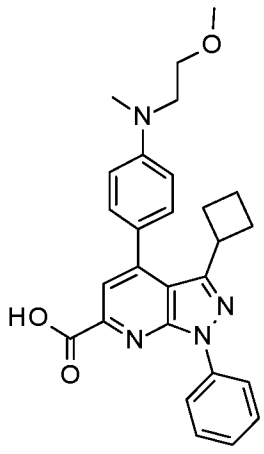
Int.	Structure	Name	SM	method	MW	Mes
A041		1-[3-(3,3-dimethylazetidin-1-yl)phenyl]-3-isopropyl-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E012	J1	525	526
A042		3-isopropyl-1-(*m*-tolyl)-4-(1-piperidyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E039	J1	378	379
A043		3-isopropyl-1-[3-(3-methoxyazetidin-1-yl)phenyl]-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E008	J1	527	528

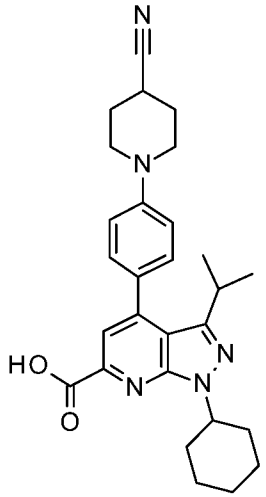
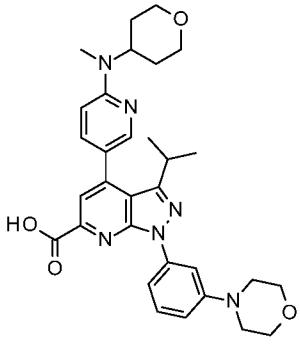
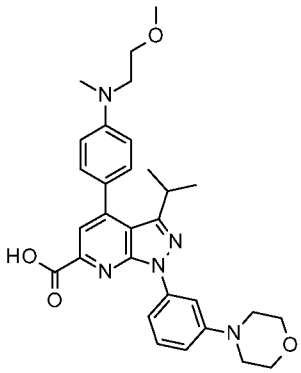
Int.	Structure	Name	SM	method	MW	Mes
A044		1-[3-(3-fluoropyrrolidin-1-yl)phenyl]-3-isopropyl-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E013	J1	529	530
A045		1-cyclohexyl-3-isopropyl-4-[6-[methyl(tetrahydropyran-4-yl)amino]-3-pyridyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E014	J1	477	478
A046		4-(4-acetamidophenyl)-1-cyclohexyl-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E021	J1	420	421

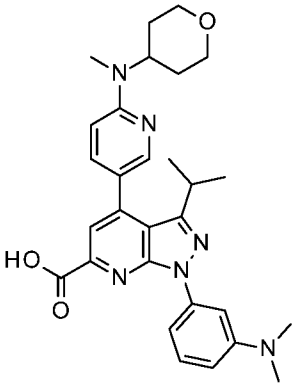
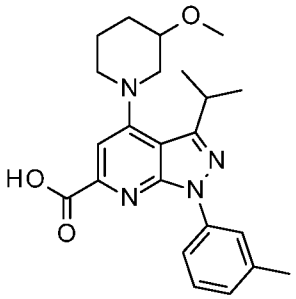
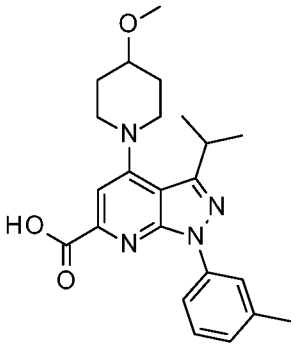
Int.	Structure	Name	SM	method	MW	Mes
A047		3-isopropyl-1-[3-[2-methoxyethyl(methyl)amino]phenyl]-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	A242	J7	529	530
A048		4-[4-(4-cyano-1-piperidyl)phenyl]-1-[3-(dimethylamino)phenyl]-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E023	J1	508	509
A049		1-[3-(dimethylamino)phenyl]-3-isopropyl-4-[4-[2-methoxyethyl(methyl)amino]phenyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E024	J1	487	488

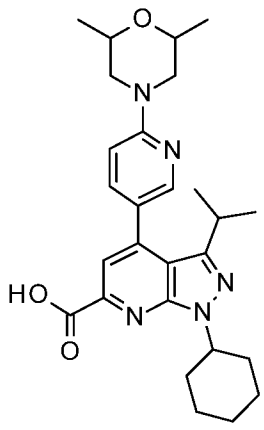
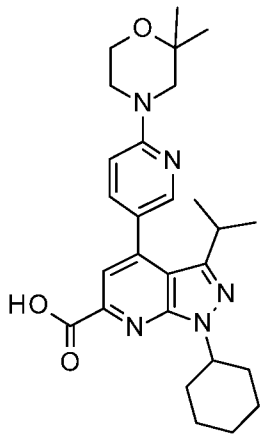
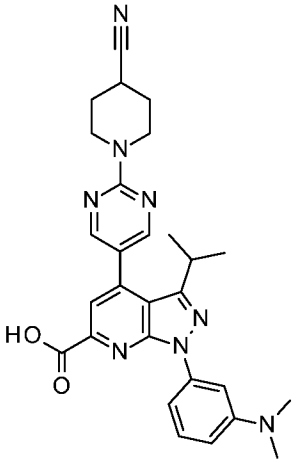
Int.	Structure	Name	SM	method	MW	Mes
A050		4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-1-[3-(dimethylamino)phenyl]-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E025	J1	509	510
A051		1-[3-(dimethylamino)phenyl]-3-isopropyl-4-[6-[2-methoxyethyl(methyl)amino]-3-pyridyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E026	J1	488	489
A052		4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-isopropyl-1-(3-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E027	J1	551	552

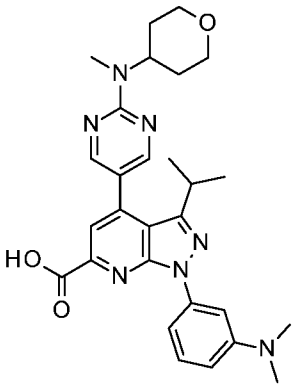
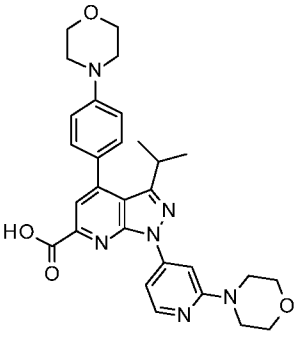
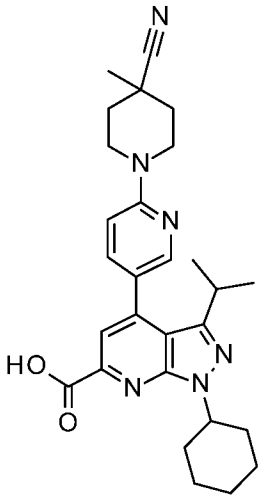
Int.	Structure	Name	SM	method	MW	Mes
A053		3-isopropyl-4-[6-[2-methoxyethyl(methyl)amino]-3-pyridyl]-1-(3-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E028	J1	530	531
A054		1-cyclohexyl-4-[6-(3,3-difluoropyrrolidin-1-yl)-3-pyridyl]-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	A250	J5	469	470
A055		3-cyclobutyl-4-[6-[2-methoxyethyl(methyl)amino]-3-pyridyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E017	J1	457	458

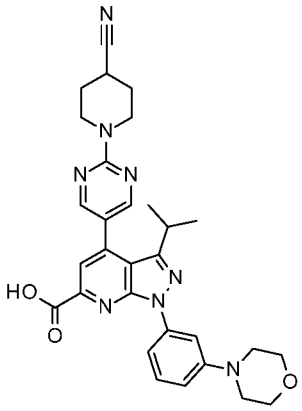
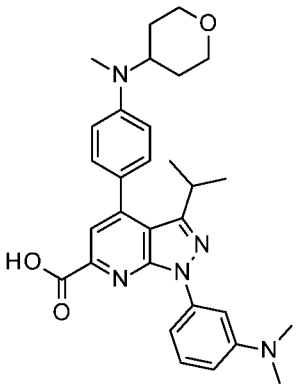
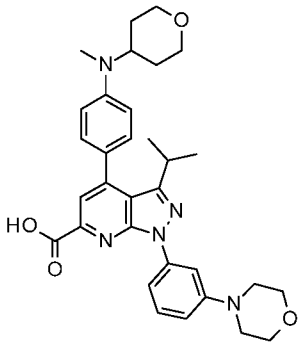
Int.	Structure	Name	SM	method	MW	Mes
A056		4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E018	J1 Specific example	478	479
A057		3-cyclobutyl-4-[6-[methyl(tetrahydropyran-4-yl)amino]-3-pyridyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E019	J1	483	484
A058		3-cyclobutyl-4-[4-[2-methoxyethyl(methyl)amino]phenyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E020	J1	456	457

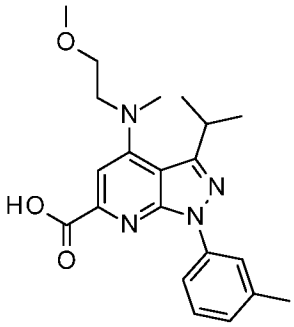
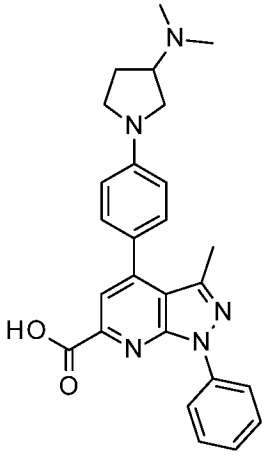
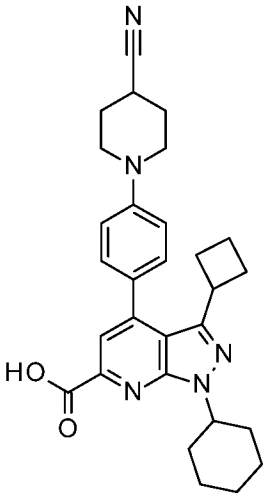
Int.	Structure	Name	SM	method	MW	Mes
A059		4-[4-(4-cyano-1-piperidyl)phenyl]-1-cyclohexyl-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E022	J1	471	472
A060		3-isopropyl-4-[6-[methyl(tetrahydropyran-4-yl)amino]-3-pyridyl]-1-(3-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E029	J1	556	557
A061		3-isopropyl-4-[4-[2-methoxyethyl(methyl)amino]phenyl]-1-(3-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E030	J1	529	530

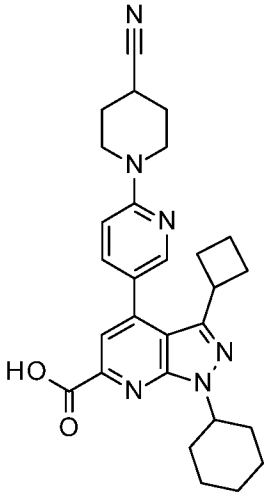
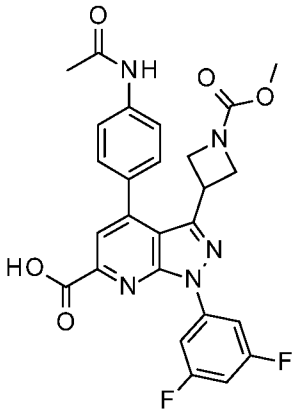
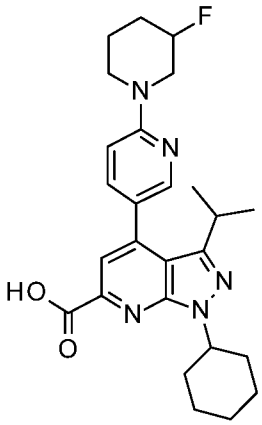
Int.	Structure	Name	SM	method	MW	Mes
A062		1-[3-(dimethylamino)phenyl]-3-isopropyl-4-[6-[methyl(tetrahydropyran-4-yl)amino]-3-pyridyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E031	J1	514	515
A063		3-isopropyl-4-(3-methoxy-1-piperidyl)-1-(*m*-tolyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E088	J1	408	409
A064		3-isopropyl-4-(4-methoxy-1-piperidyl)-1-(*m*-tolyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E048	J1	408	409

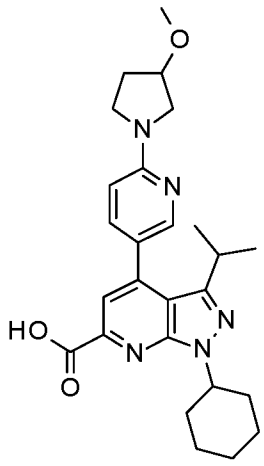
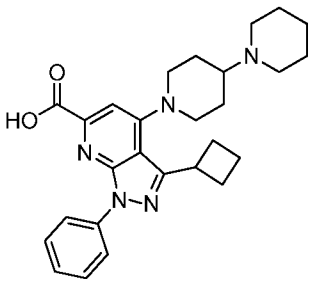
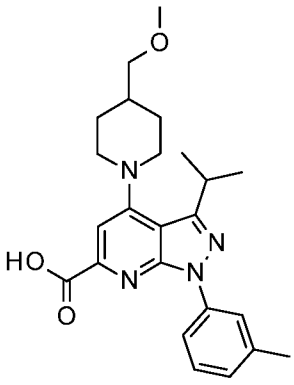
Int.	Structure	Name	SM	method	MW	Mes
A065		1-cyclohexyl-4-[6-(2,6-dimethylmorpholin-4-yl)-3-pyridyl]-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	A250	J5 Specific example	477	478
A066		1-cyclohexyl-4-[6-(2,2-dimethylmorpholin-4-yl)-3-pyridyl]-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	A250	J5	477	478
A067		4-[2-(4-cyano-1-piperidyl)pyrimidin-5-yl]-1-[3-(dimethylamino)phenyl]-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E034	J1	510	511

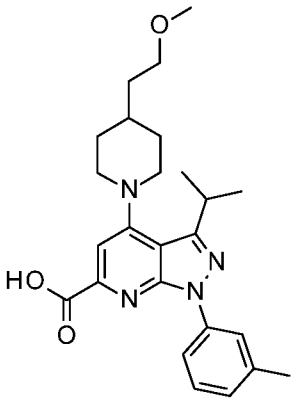
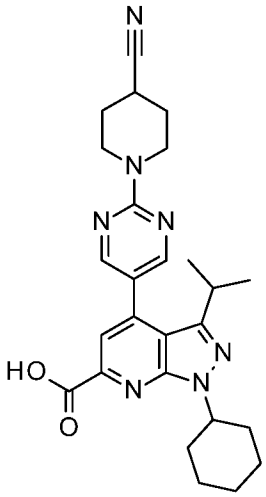
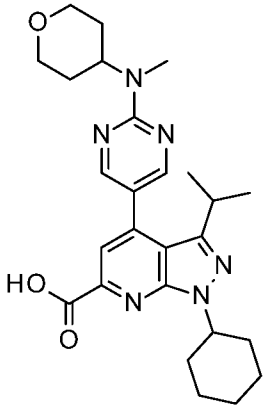
Int.	Structure	Name	SM	method	MW	Mes
A068		1-[3-(dimethylamino)phenyl]-3-isopropyl-4-[2-[methyl(tetrahydropyran-4-yl)amino]pyrimidin-5-yl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E032	J1	515	516
A069		3-isopropyl-4-(4-morpholinophenyl)-1-(2-morpholino-4-pyridyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E066	J1	528	529
A070		4-[6-(4-cyano-4-methyl-1-piperidyl)-3-pyridyl]-1-cyclohexyl-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	A250	J5	486	487

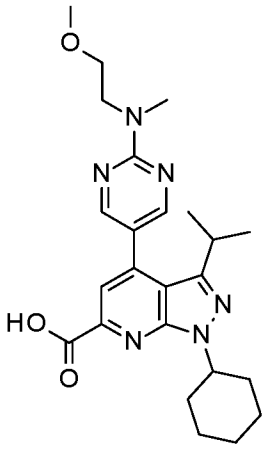
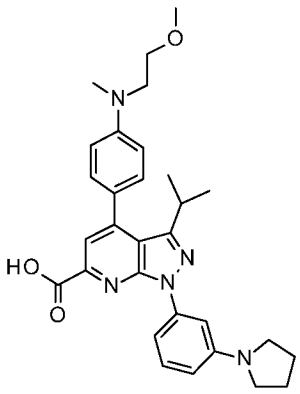
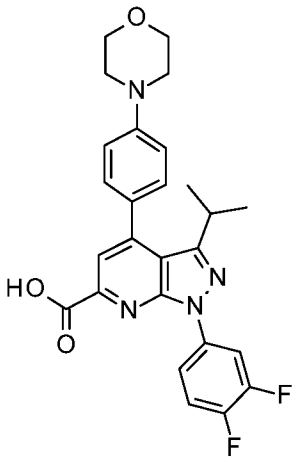
Int.	Structure	Name	SM	method	MW	Mes
A071		4-[2-(4-cyano-1-piperidyl)pyrimidin-5-yl]-3-isopropyl-1-(3-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E037	J1	552	553
A072		1-[3-(dimethylamino)phenyl]-3-isopropyl-4-[4-[methyl(tetrahydropyran-4-yl)amino]phenyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E035	J1	513	514
A073		3-isopropyl-4-[4-[methyl(tetrahydropyran-4-yl)amino]phenyl]-1-(3-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E036	J1	555	556

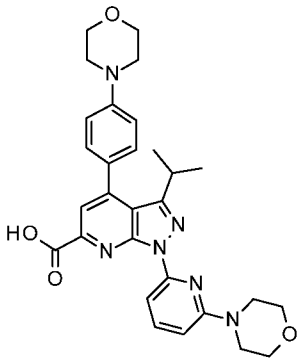
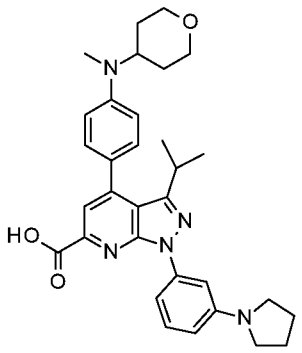
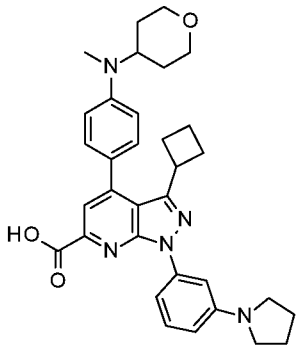
Int.	Structure	Name	SM	method	MW	Mes
A074		3-isopropyl-4-[2-methoxyethyl(methyl)amino]-1-(*m*-tolyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E094	J1	382	383
A075		4-[4-[3-(dimethylamino)pyrrolidin-1-yl]phenyl]-3-methyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E038	J1	441	442
A076		4-[4-(4-cyano-1-piperidyl)phenyl]-3-cyclobutyl-1-cyclohexyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E040	J1	483	484

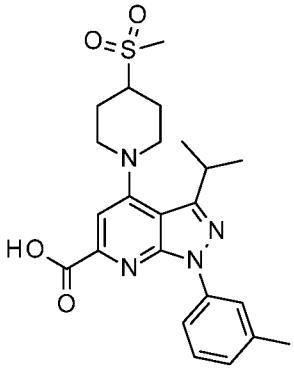
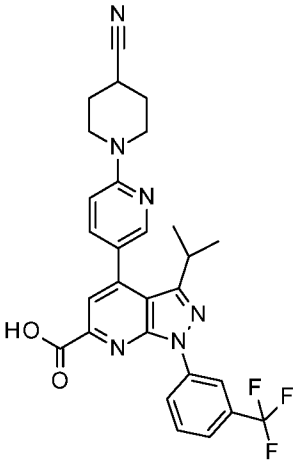
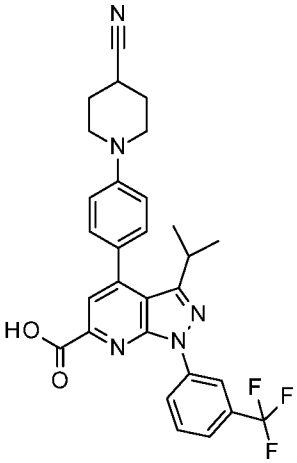
Int.	Structure	Name	SM	method	MW	Mes
A077		4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-cyclobutyl-1-cyclohexyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E041	J1	484	485
A078		4-(4-acetamidophenyl)-1-(3,5-difluorophenyl)-3-(1-methoxycarbonyl azetidin-3-yl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E042	J1	521	522
A079		1-cyclohexyl-4-[6-(3-fluoro-1-piperidyl)-3-pyridyl]-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	A250	J5	465	466

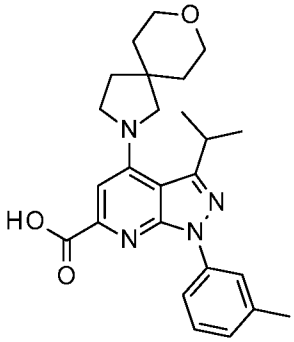
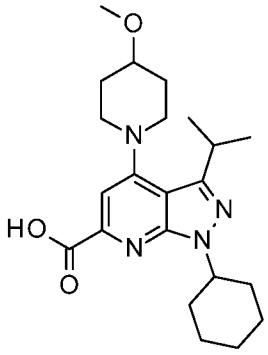
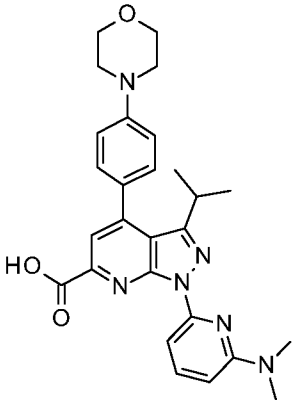
Int.	Structure	Name	SM	method	MW	Mes
A080		1-cyclohexyl-3-isopropyl-4-[6-(3-methoxypyrrolidin-1-yl)-3-pyridyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	A250	J5	463	464
A081		3-cyclobutyl-1-phenyl-4-[4-(1-piperidyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10	J10 Specific example	459	460
A082		3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]-1-(*m*-tolyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E082	J1	422	423

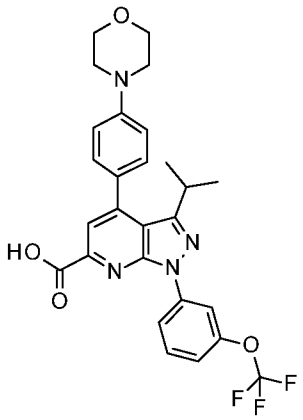
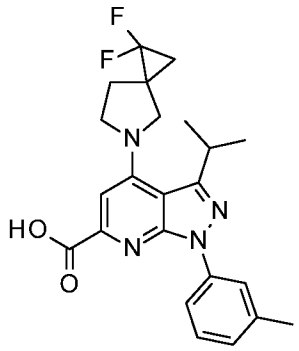
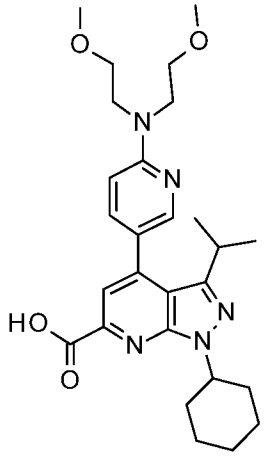
Int.	Structure	Name	SM	method	MW	Mes
A083		3-isopropyl-4-[4-(2-methoxyethyl)-1-piperidyl]-1-(*m*-tolyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E087	J1	436	437
A084		4-[2-(4-cyano-1-piperidyl)pyrimidin-5-yl]-1-cyclohexyl-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E049	J1	473	474
A085		1-cyclohexyl-3-isopropyl-4-[2-[methyl(tetrahydropyran-4-yl)amino]pyrimidin-5-yl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E051	J1	478	479

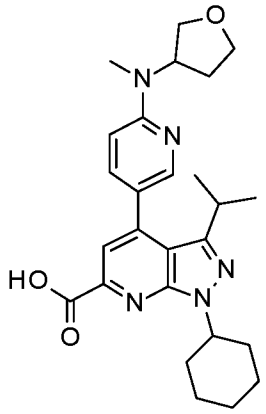
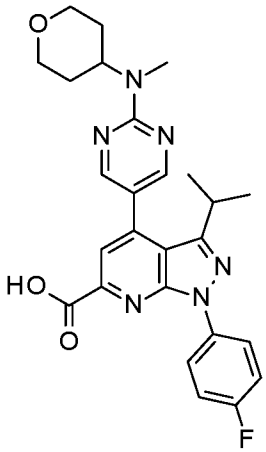
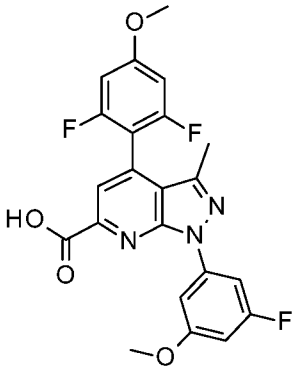
Int.	Structure	Name	SM	method	MW	Mes
A086		1-cyclohexyl-3-isopropyl-4-[2-[2-methoxyethyl(methyl)amino]pyrimidin-5-yl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E050	J1	452	453
A087		3-isopropyl-4-[4-[2-methoxyethyl(methyl)amino]phenyl]-1-(3-pyrrolidin-1-ylphenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E045	J1	513	514
A088		1-(3,4-difluorophenyl)-3-isopropyl-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E057	J1	478	479

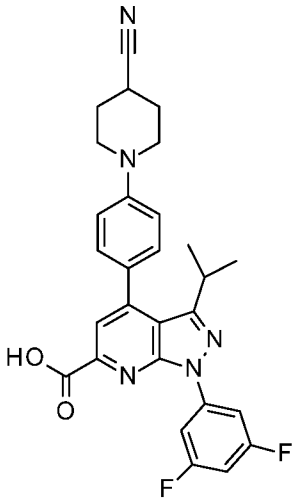
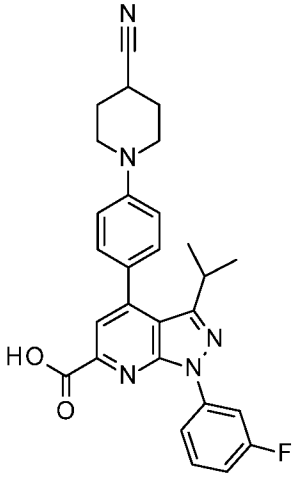
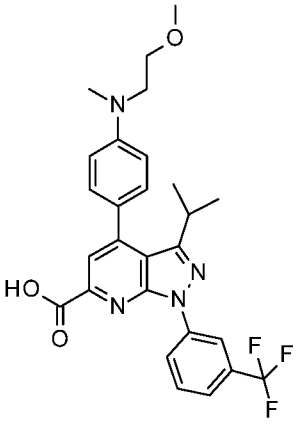
Int.	Structure	Name	SM	method	MW	Mes
A089		3-isopropyl-4-(4-morpholinophenyl)-1-(6-morpholino-2-pyridyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E058	J1	528	529
A090		3-isopropyl-4-[4-[methyl(tetrahydropyran-4-yl)amino]phenyl]-1-(3-pyrrolidin-1-ylphenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E046	J1	539	540
A091		3-cyclobutyl-4-[4-[methyl(tetrahydropyran-4-yl)amino]phenyl]-1-(3-pyrrolidin-1-ylphenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E047	J1	551	552

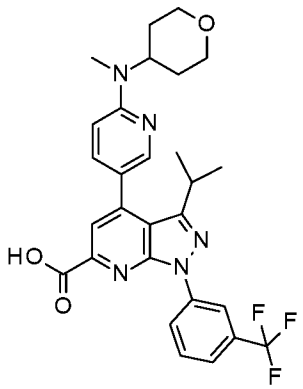
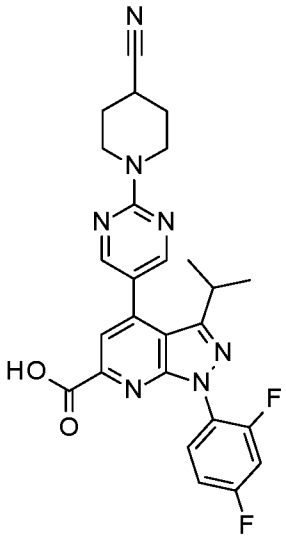
Int.	Structure	Name	SM	method	MW	Mes
A092		3-isopropyl-4-(4-methylsulfonyl-1-piperidyl)-1-(*m*-tolyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E089	J1	456	457
A093		4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-isopropyl-1-[3-(trifluoromethyl)phenyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E052	J1	534	535
A094		4-[4-(4-cyano-1-piperidyl)phenyl]-3-isopropyl-1-[3-(trifluoromethyl)phenyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E065	J1	533	534

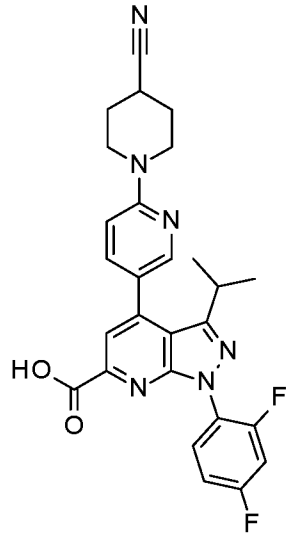
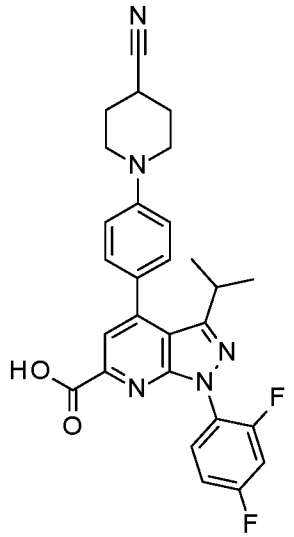
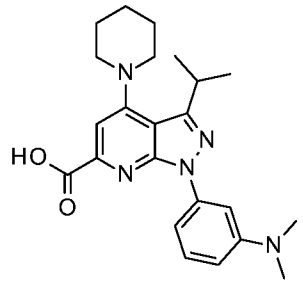
Int.	Structure	Name	SM	method	MW	Mes
A095		3-isopropyl-1-(*m*-tolyl)-4-(8-oxa-3-azaspiro[4.5]decan-3-yl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E095	J1	434	435
A096		1-cyclohexyl-3-isopropyl-4-(4-methoxy-1-piperidyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E076	J1	400	401
A097		1-[6-(dimethylamino)-2-pyridyl]-3-isopropyl-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E053	J1	486	487

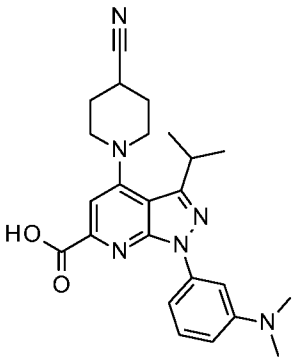
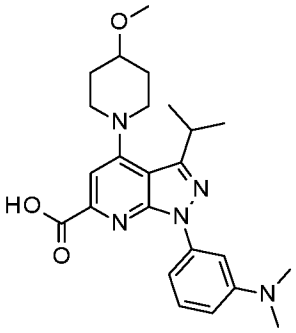
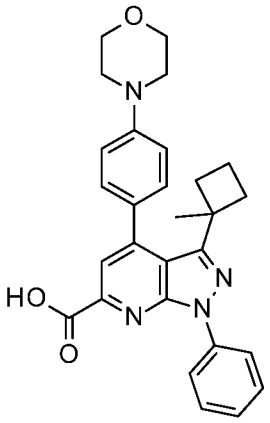
Int.	Structure	Name	SM	method	MW	Mes
A098		3-isopropyl-4-(4-morpholinophenyl)-1-[3-(trifluoromethoxy)phenyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E054	J1	526	527
A099		4-(2,2-difluoro-6-azaspiro[2.4]heptan-6-yl)-3-isopropyl-1-(*m*-tolyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E075	J1	426	427
A100		4-[6-[bis(2-methoxyethyl)amino]-3-pyridyl]-1-cyclohexyl-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	A250	J5	495	496

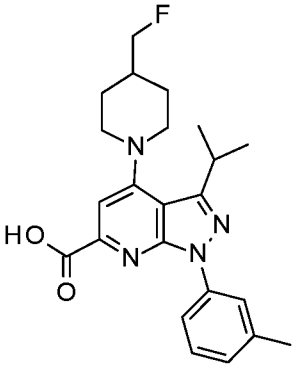
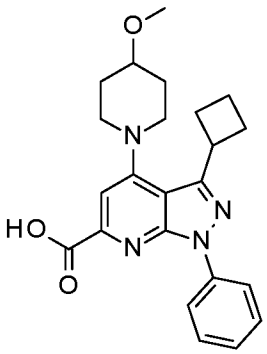
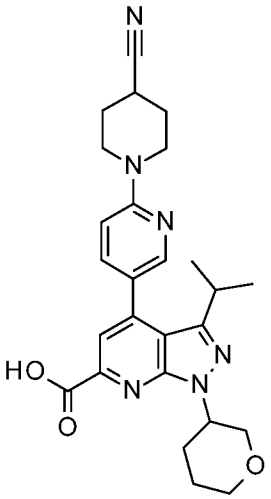
Int.	Structure	Name	SM	method	MW	Mes
A101		1-cyclohexyl-3-isopropyl-4-[6-[methyl(tetrahydrofuran-3-yl)amino]-3-pyridyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	A250	J5	463	464
A102		1-(4-fluorophenyl)-3-isopropyl-4-[2-[methyl(tetrahydropyran-4-yl)amino]pyrimidin-5-yl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E064	J1	490	491
A103		4-(2,6-difluoro-4-methoxy-phenyl)-1-(3-fluoro-5-methoxy-phenyl)-3-methyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E059	J1	443	444

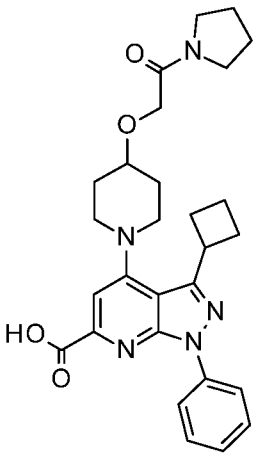
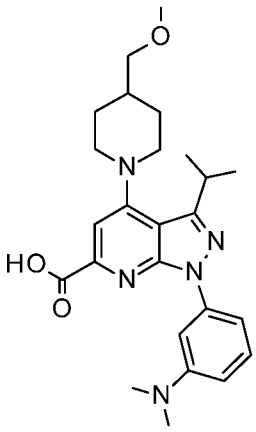
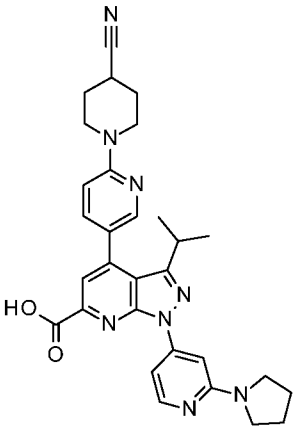
Int.	Structure	Name	SM	method	MW	Mes
A104		4-[4-(4-cyano-1-piperidyl)phenyl]-1-(3,5-difluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E060	J1	501	502
A105		4-[4-(4-cyano-1-piperidyl)phenyl]-1-(3-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E061	J1	483	484
A106		3-isopropyl-4-[4-[2-methoxyethyl(methyl)amino]phenyl]-1-[3-(trifluoromethyl)phenyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E062	J1	512	513

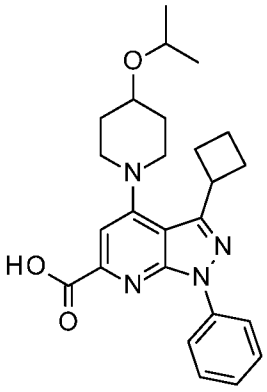
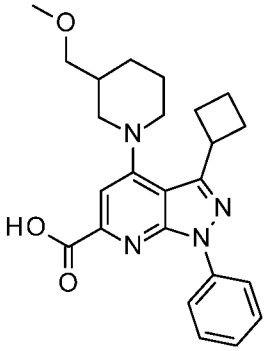
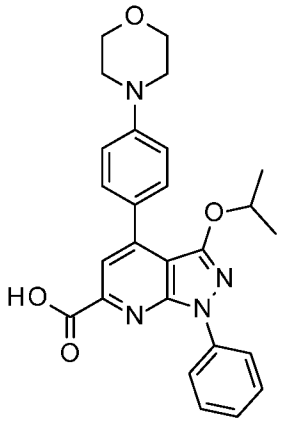
Int.	Structure	Name	SM	method	MW	Mes
A107		3-isopropyl-4-[6-[methyl(tetrahydropyran-4-yl)amino]-3-pyridyl]-1-[3-(trifluoromethyl)phenyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E063	J1	539	540
A108		4-[2-(4-cyano-1-piperidyl)pyrimidin-5-yl]-1-(2,4-difluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E068	J1	503	504

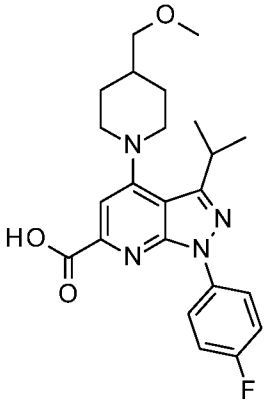
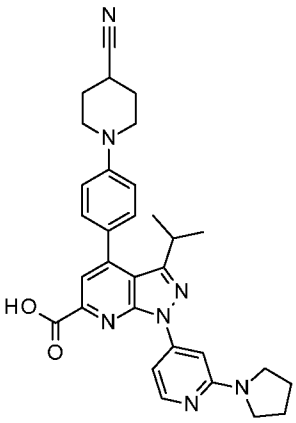
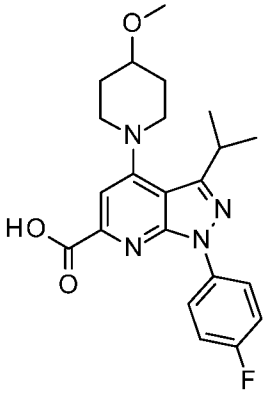
Int.	Structure	Name	SM	method	MW	Mes
A109		4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-1-(2,4-difluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E069	J1	502	503
A110		4-[4-(4-cyano-1-piperidyl)phenyl]-1-(2,4-difluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E070	J1	501	502
A111		1-[3-(dimethylamino)phenyl]-3-isopropyl-4-(1-piperidyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E083	J1	407	408

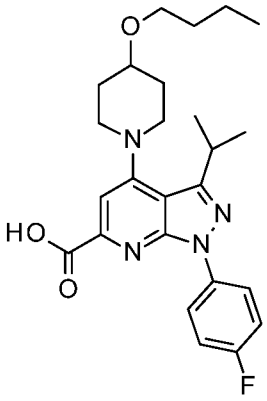
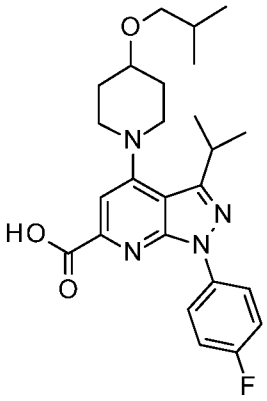
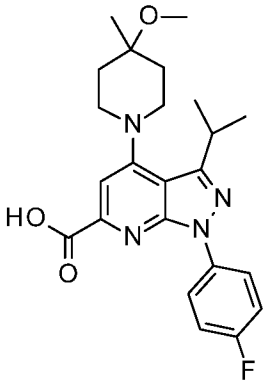
Int.	Structure	Name	SM	method	MW	Mes
A112		4-(4-cyano-1-piperidyl)-1-[3-(dimethylamino)phenyl]-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E086	J1	432	433
A113		1-[3-(dimethylamino)phenyl]-3-isopropyl-4-(4-methoxy-1-piperidyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E081	J1	437	438
A114		3-(1-methylcyclobutyl)-4-(4-morpholinophenyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E067	J1	468	469

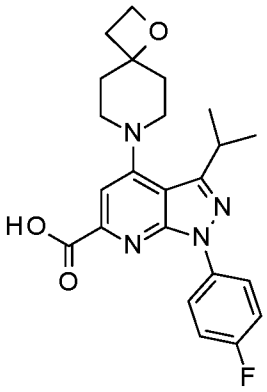
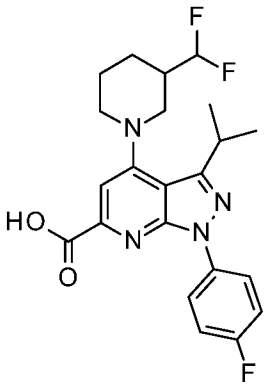
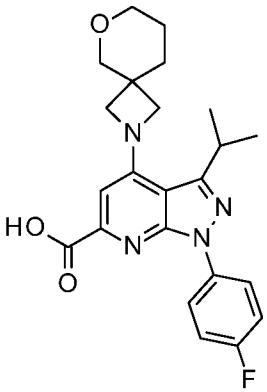
Int.	Structure	Name	SM	method	MW	Mes
A115		4-[4-(fluoromethyl)-1-piperidyl]-3-isopropyl-1-(*m*-tolyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP16	J4	410	411
A116		3-cyclobutyl-4-(4-methoxy-1-piperidyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E071	J1	406	407
A117		4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-isopropyl-1-tetrahydropyran-3-yl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E073	J1	474	475

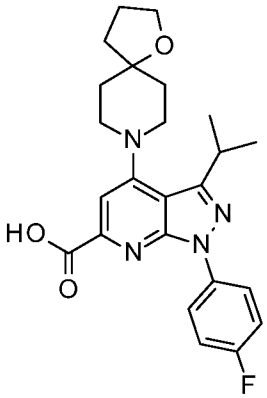
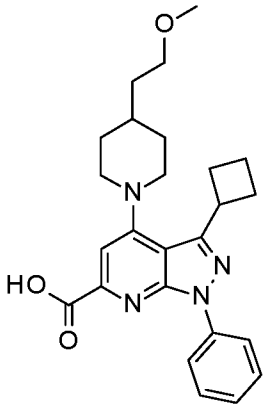
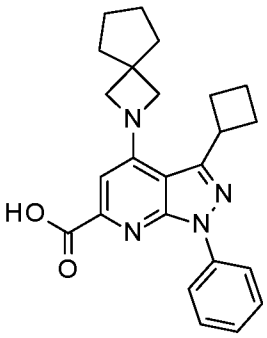
Int.	Structure	Name	SM	method	MW	Mes
A118		3-cyclobutyl-4-[4-(2-oxo-2-pyrrolidin-1-yl-ethoxy)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E080	J1	503	504
A119		1-[3-(dimethylamino)phenyl]-3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E072	J1	451	452
A120		4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-isopropyl-1-(2-pyrrolidin-1-yl-4-pyridyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E084	J1	536	537

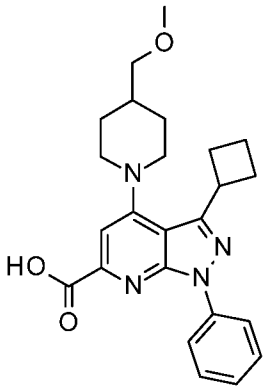
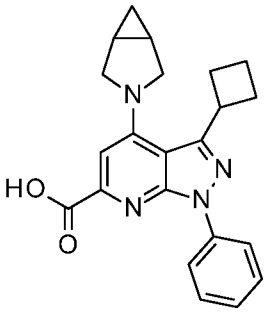
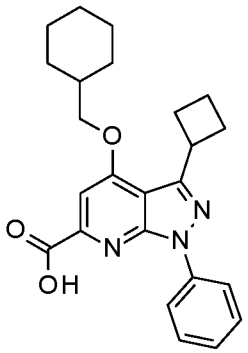
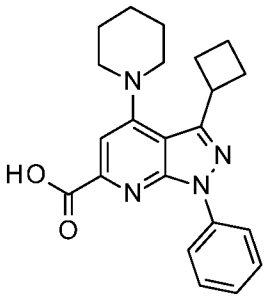
Int.	Structure	Name	SM	method	MW	Mes
A121		3-cyclobutyl-4-(4-isopropoxy-1-piperidyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E077	J1	434	435
A122		3-cyclobutyl-4-[3-(methoxymethyl)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E079	J1	420	421
A123		3-isopropoxy-4-(4-morpholinophenyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E090	J1	458	459

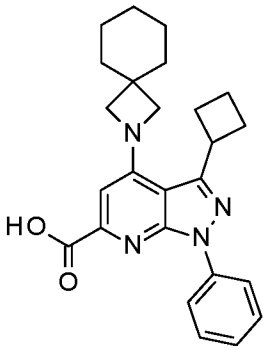
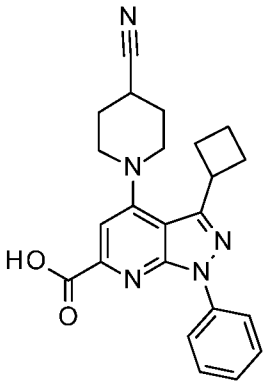
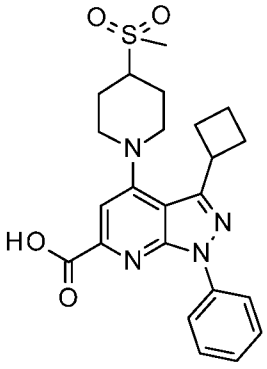
Int.	Structure	Name	SM	method	MW	Mes
A124		1-(4-fluorophenyl)-3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E092	J1	426	427
A125		4-[4-(4-cyano-1-piperidyl)phenyl]-3-isopropyl-1-(2-pyrrolidin-1-yl-4-pyridyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E093	J1	535	536
A126		1-(4-fluorophenyl)-3-isopropyl-4-(4-methoxy-1-piperidyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E091	J1	412	413

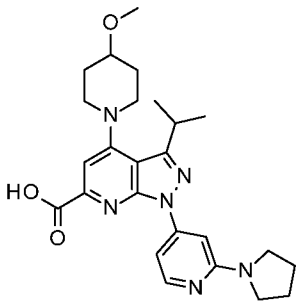
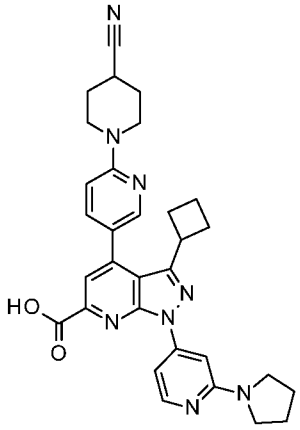
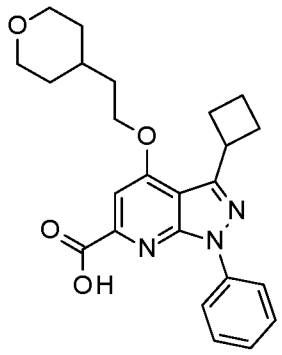
Int.	Structure	Name	SM	method	MW	Mes
A127		4-(4-butoxy-1-piperidyl)-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E096	J1	454	455
A128		1-(4-fluorophenyl)-4-(4-isobutoxy-1-piperidyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E098	J1	454	455
A129		1-(4-fluorophenyl)-3-isopropyl-4-(4-methoxy-4-methyl-1-piperidyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E097	J1	426	427

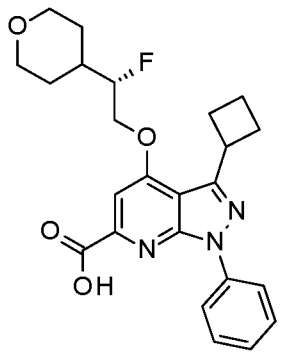
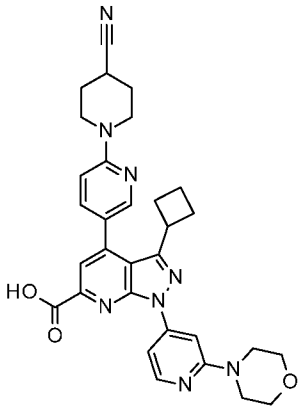
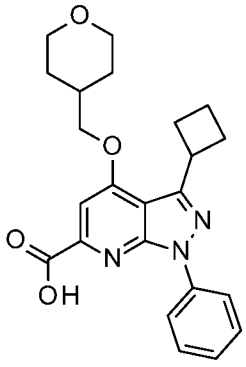
Int.	Structure	Name	SM	method	MW	Mes
A130		1-(4-fluorophenyl)-3-isopropyl-4-(3-oxa-7-azaspiro[3.5]nonan-7-yl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E099	J1	424	425
A131		4-[3-(difluoromethyl)-1-piperidyl]-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E100	J1	432	433
A132		1-(4-fluorophenyl)-3-isopropyl-4-(8-oxa-2-azaspiro[3.5]nonan-2-yl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E101	J1	424	425

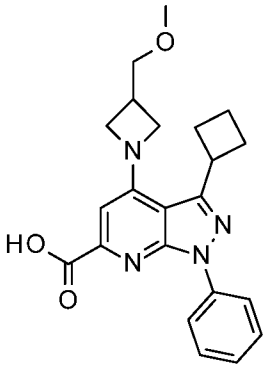
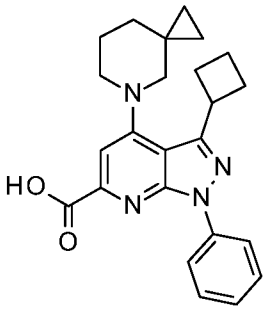
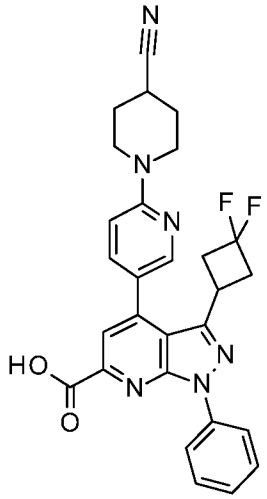
Int.	Structure	Name	SM	method	MW	Mes
A133		1-(4-fluorophenyl)-3-isopropyl-4-(4-oxa-8-azaspiro[4.5]decan-8-yl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E102	J1	438	439
A134		3-cyclobutyl-4-[4-(2-methoxyethyl)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E104	J1	434	435
A135		4-(2-azaspiro[3.4]octan-2-yl)-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E105	J1	402	403

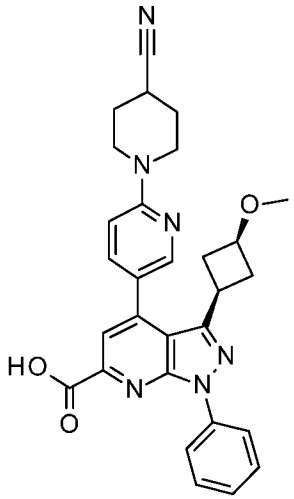
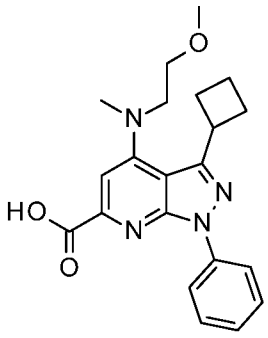
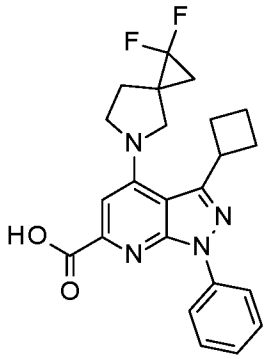
Int.	Structure	Name	SM	method	MW	Mes
A136		3-cyclobutyl-4-[4-(methoxymethyl)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E106	J1	420	421
A137		4-(3-azabicyclo[3.1.0]hexan-3-yl)-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E107	J1	374	375
A138		3-cyclobutyl-4-(cyclohexylmethoxy)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10	J3	405	406
A139		3-cyclobutyl-1-phenyl-4-(1-piperidyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E103	J1	376	377

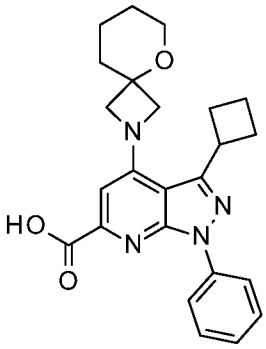
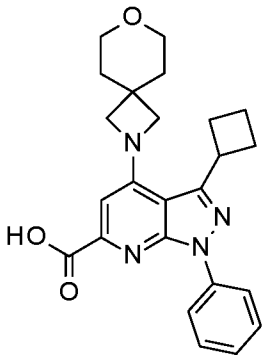
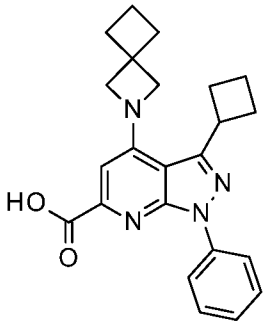
Int.	Structure	Name	SM	method	MW	Mes
A140		4-(2-azaspiro[3.5]nonan-2-yl)-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E115	J1	416	417
A141		4-(4-cyano-1-piperidyl)-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E114	J1	401	402
A142		3-cyclobutyl-4-(4-methylsulfonyl-1-piperidyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E113	J1	454	455

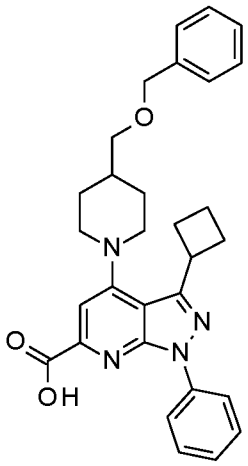
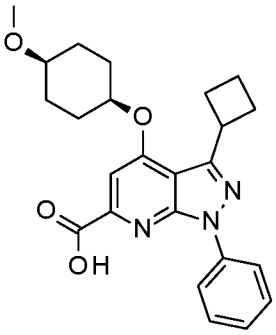
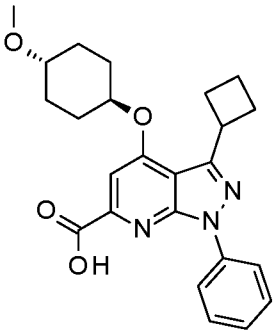
Int.	Structure	Name	SM	method	MW	Mes
A143		3-isopropyl-4-(4-methoxy-1-piperidyl)-1-(2-pyrrolidin-1-yl-4-pyridyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E110	J1	464	465
A144		4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-cyclobutyl-1-(2-pyrrolidin-1-yl-4-pyridyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E112	J1	548	549
A145		3-cyclobutyl-1-phenyl-4-(2-tetrahydropyran-4-ylethoxy)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10	J3	421	422

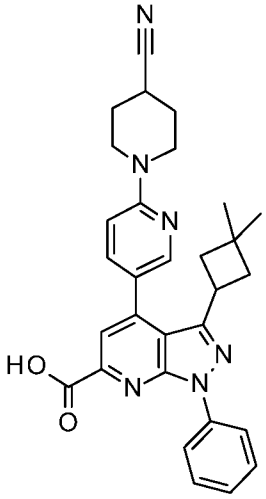
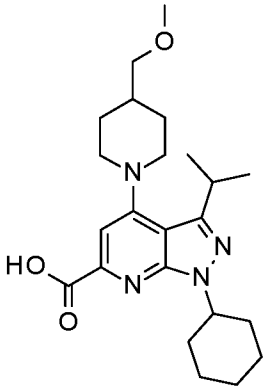
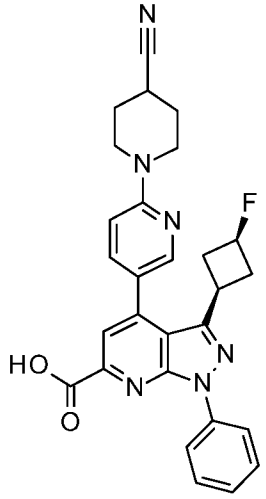
Int.	Structure	Name	SM	method	MW	Mes
A146		3-cyclobutyl-4-[(2S)-2-fluoro-2-tetrahydropyran-4-yl-ethoxy]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10, ALC01	J3	439	440
A147		4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-cyclobutyl-1-(2-morpholino-4-pyridyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E121	J1	564	565
A148		3-cyclobutyl-1-phenyl-4-(tetrahydropyran-4-ylmethoxy)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10	J3 Specific example	407	408

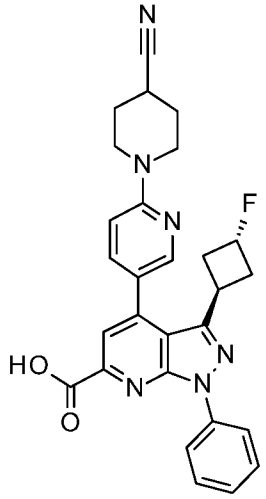
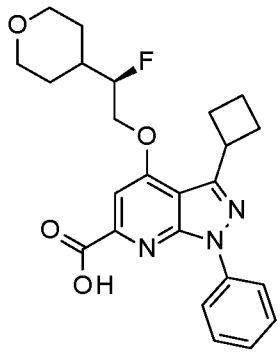
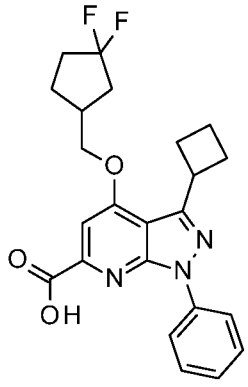
Int.	Structure	Name	SM	method	MW	Mes
A149		3-cyclobutyl-4-[3-(methoxymethyl)azetidin-1-yl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E116	J1	392	393
A150		4-(7-azaspiro[2.5]octan-7-yl)-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E125	J1	402	403
A151		4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-(3,3-difluorocyclobutyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E118	J1	514	515

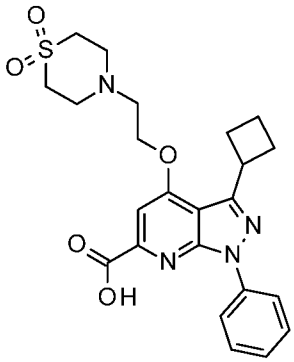
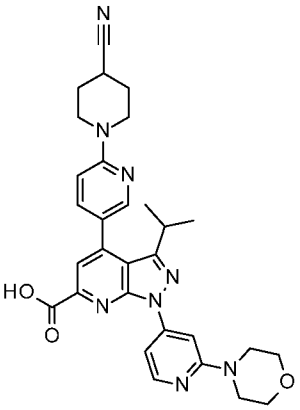
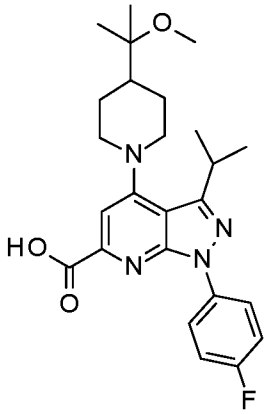
Int.	Structure	Name	SM	method	MW	Mes
A152		4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-[(1*s*,3*s*)-3-methoxycyclobutyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E117	J1	508	509
A153		3-cyclobutyl-4-[2-methoxyethyl(methyl)amino]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E126	J1	380	381
A154		3-cyclobutyl-4-(2,2-difluoro-6-azaspiro[2.4]heptan-6-yl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E122	J1	424	425

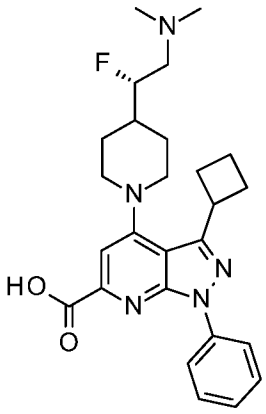
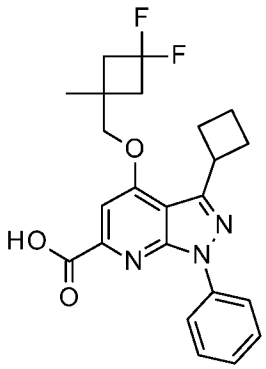
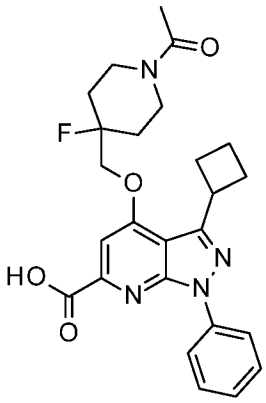
Int.	Structure	Name	SM	method	MW	Mes
A155		3-cyclobutyl-4-(9-oxa-2-azaspiro[3.5]nonan-2-yl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E123	J1	418	419
A156		3-cyclobutyl-4-(7-oxa-2-azaspiro[3.5]nonan-2-yl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E124	J1	418	419
A157		4-(6-azaspiro[3.3]heptan-6-yl)-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E128	J1	388	389

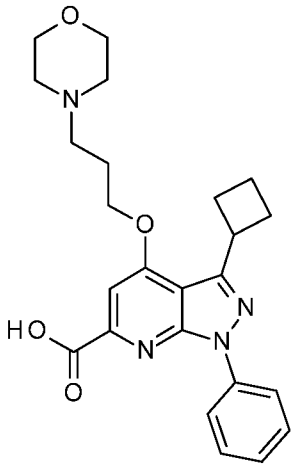
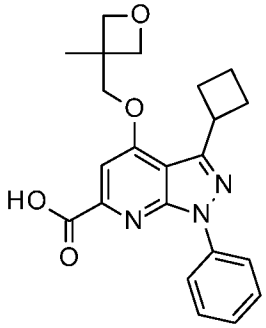
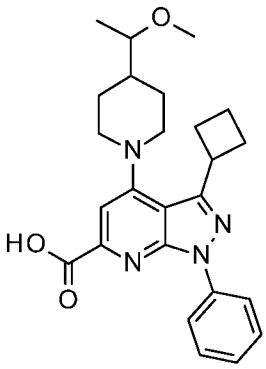
Int.	Structure	Name	SM	method	MW	Mes
A158		4-[4-(benzyloxymethyl)-1-piperidyl]-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E127	J1	496	497
A159		3-cyclobutyl-4-{[(1*s*,4*s*)-4-methoxycyclohexyl]oxy}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10	J3	421	422
A160		3-cyclobutyl-4-{[(1*r*,4*r*)-4-methoxycyclohexyl]oxy}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10	J3	421	422

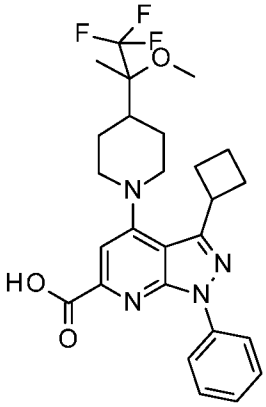
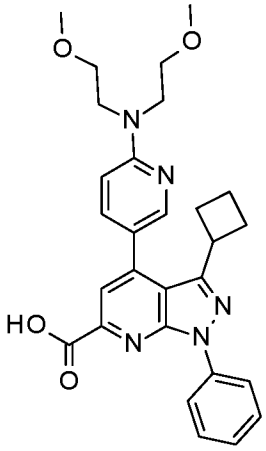
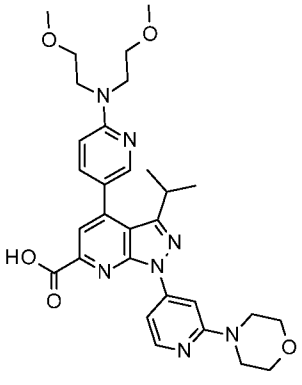
Int.	Structure	Name	SM	method	MW	Mes
A161		4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-(3,3-dimethylcyclobutyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E119	J1	506	507
A162		1-cyclohexyl-3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E134	J8 Specific example	414	415
A163		4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-(3-fluorocyclobutyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (cis)	A258	Separation by prep HPLC	496	497

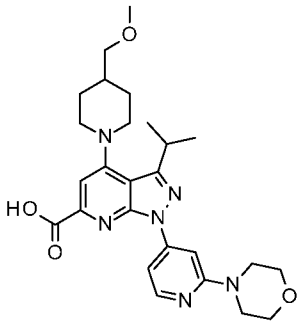
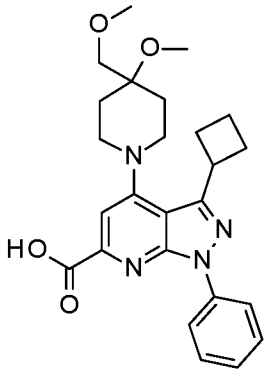
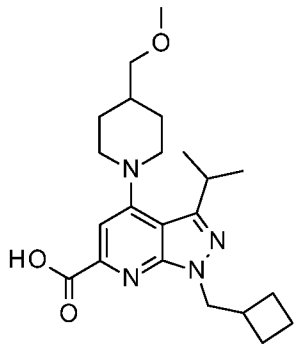
Int.	Structure	Name	SM	method	MW	Mes
A164		4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-(3-fluorocyclobutyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid trans	A258	Separation by prep HPLC	496	497
A165		3-cyclobutyl-4-[(2R)-2-fluoro-2-tetrahydropyran-4-yl-ethoxy]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10, ALC02	J3	439	440
A166		3-cyclobutyl-4-[(3,3-difluorocyclopentyl)methoxy]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10	J3	427	428

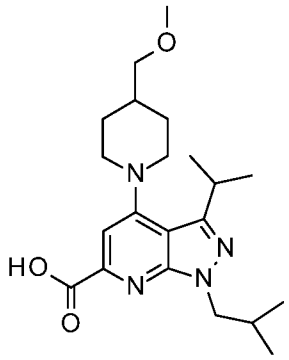
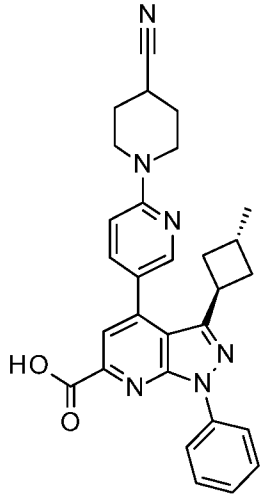
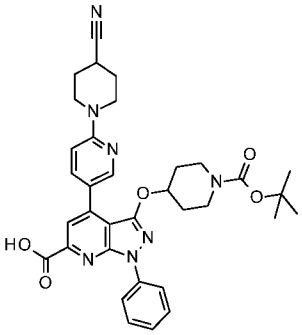
Int.	Structure	Name	SM	method	MW	Mes
A167		3-cyclobutyl-4-[2-(1,1-dioxo-1,4-thiazinan-4-yl)ethoxy]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10	J3	470	471
A168		4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-isopropyl-1-(2-morpholino-4-pyridyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E138	J1	552	553
A169		1-(4-fluorophenyl)-3-isopropyl-4-[4-(1-methoxy-1-methyl-ethyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E136	J8	454	455

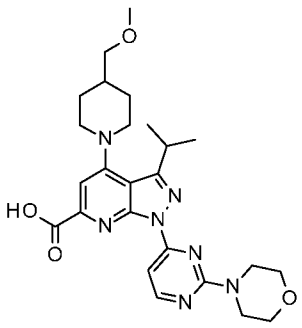
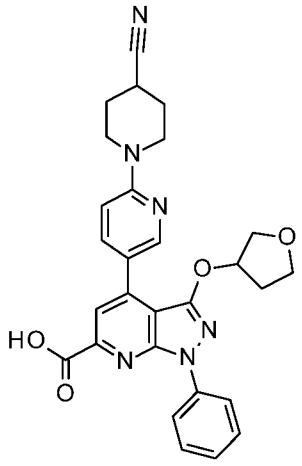
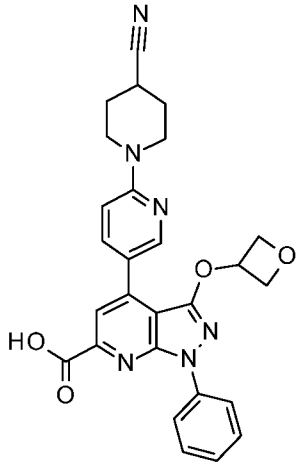
Int.	Structure	Name	SM	method	MW	Mes
A170		3-cyclobutyl-4-[4-[(1S)-2-(dimethylamino)-1-fluoro-ethyl]-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E135	J1	465	466
A171		3-cyclobutyl-4-[(3,3-difluoro-1-methyl-cyclobutyl)methoxy]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10	J3	427	428
A172		4-[(1-acetyl-4-fluoro-4-piperidyl)methoxy]-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10	J3	466	467

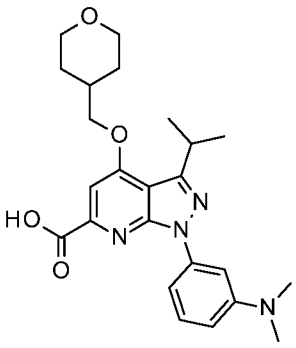
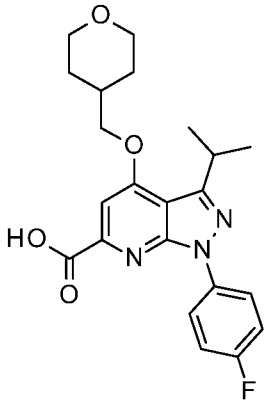
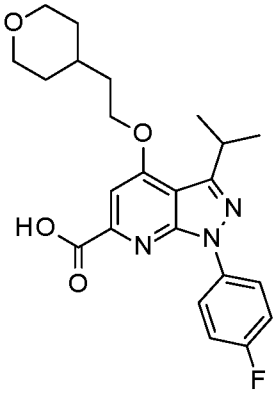
Int.	Structure	Name	SM	method	MW	Mes
A173		3-cyclobutyl-4-(3-morpholinopropoxy)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10	J3 Specific example	436	437
A174		3-cyclobutyl-4-[(3-methyloxetan-3-yl)methoxy]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10	J3	393	394
A175		3-cyclobutyl-4-[4-(1-methoxyethyl)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E143	J8	434	435

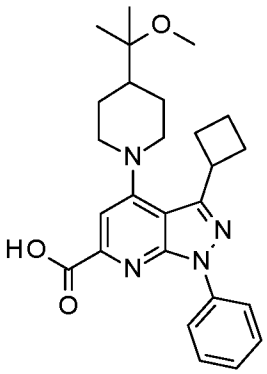
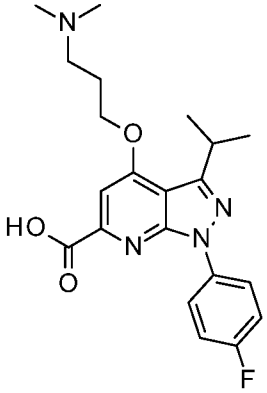
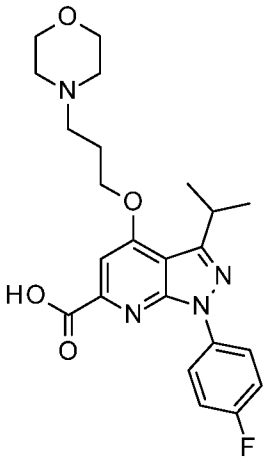
Int.	Structure	Name	SM	method	MW	Mes
A176		3-cyclobutyl-1-phenyl-4-[4-(2,2,2-trifluoro-1-methoxy-1-methyl-ethyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E144	J8	502	503
A177		4-[6-[bis(2-methoxyethyl)amino]-3-pyridyl]-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E145	J1	501	502
A178		4-[6-[bis(2-methoxyethyl)amino]-3-pyridyl]-3-isopropyl-1-(2-morpholino-4-pyridyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E149	J1	575	576

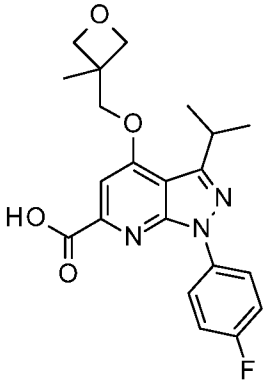
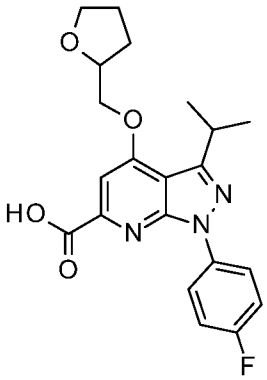
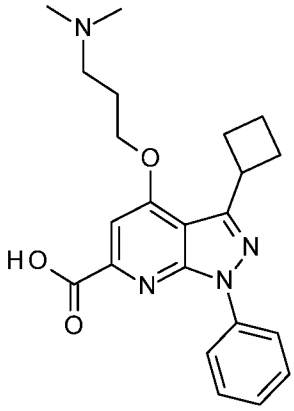
Int.	Structure	Name	SM	method	MW	Mes
A179		3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]-1-(2-morpholino-4-pyridyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E147	J6 Specific example	494	495
A180		3-cyclobutyl-4-[4-methoxy-4-(methoxymethyl)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E146	J8	450	451
A181		1-(cyclobutylmethyl)-3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E154	J1	400	401

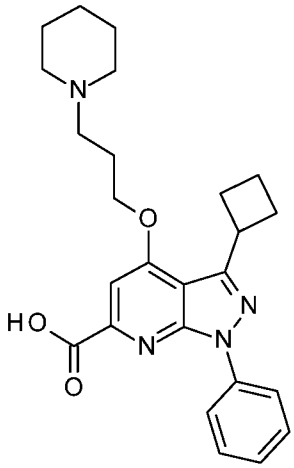
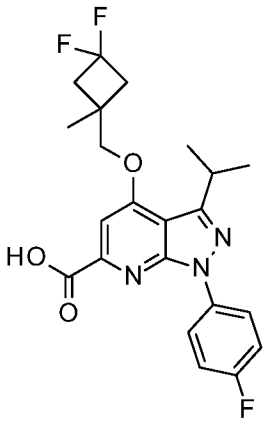
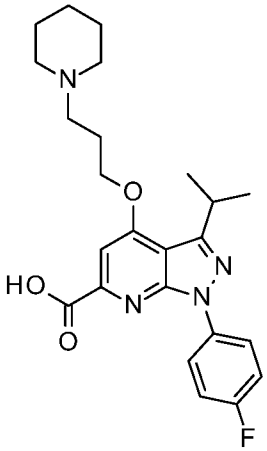
Int.	Structure	Name	SM	method	MW	Mes
A182		1-isobutyl-3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E155	J1	388	389
A183		4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-[(1*r*,3*r*)-3-methylcyclobutyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E151	J1	492	493
A184		3-[(1-*tert*-butoxycarbonyl-4-piperidyl)oxy]-4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E152	J1	623	624

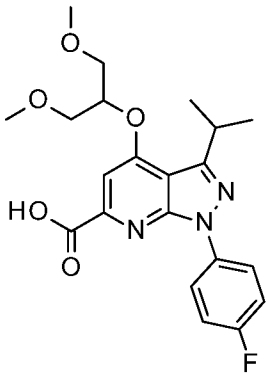
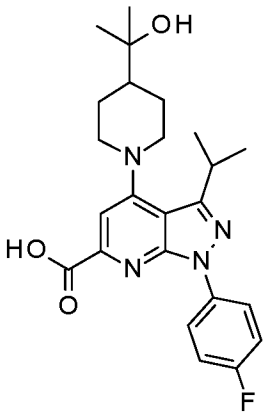
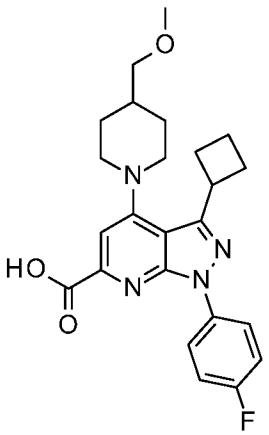
Int.	Structure	Name	SM	method	MW	Mes
A185		3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]-1-(2-morpholinopyrimidin-4-yl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E160	J1	495	496
A186		4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-1-phenyl-3-tetrahydrofuran-3-yloxy-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E159	J1	510	511
A187		4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-(oxetan-3-yloxy)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E164	J1	496	497

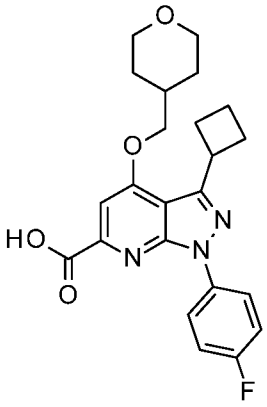
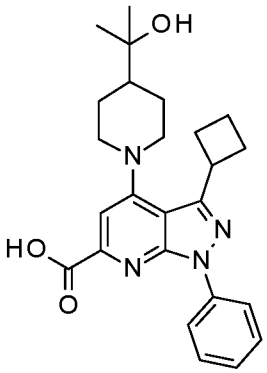
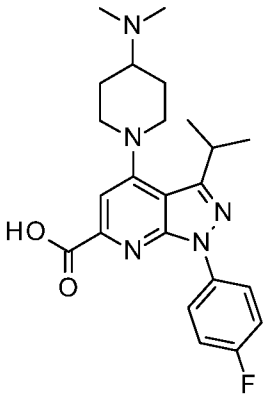
Int.	Structure	Name	SM	method	MW	Mes
A188		1-[3-(dimethylamino)phenyl]-3-isopropyl-4-(tetrahydropyran-4-ylmethoxy)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP07	J3	438	439
A189		1-(4-fluorophenyl)-3-isopropyl-4-(tetrahydropyran-4-ylmethoxy)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP11	J3	413	414
A190		1-(4-fluorophenyl)-3-isopropyl-4-(2-tetrahydropyran-4-ylethoxy)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP11	J3	427	428

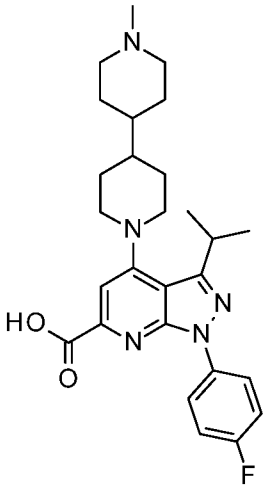
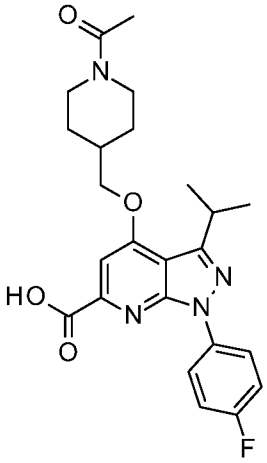
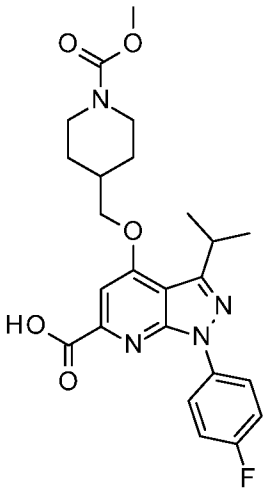
Int.	Structure	Name	SM	method	MW	Mes
A191		3-cyclobutyl-4-[4-(1-methoxy-1-methyl-ethyl)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E163	J8	448	449
A192		4-[3-(dimethylamino)propoxy]-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP11	J3	400	401
A193		1-(4-fluorophenyl)-3-isopropyl-4-(3-morpholinopropoxy)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP11	J3	442	443

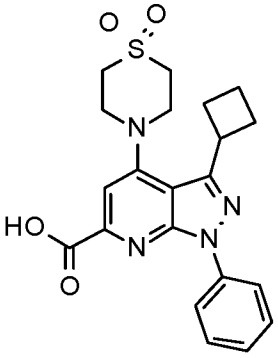
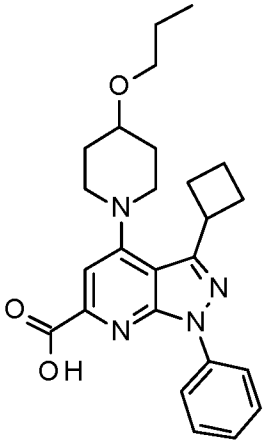
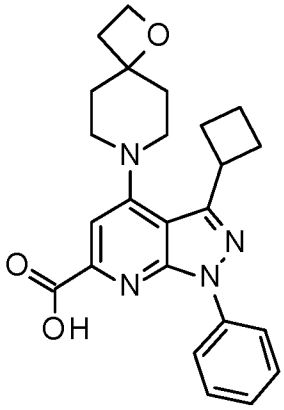
Int.	Structure	Name	SM	method	MW	Mes
A194		1-(4-fluorophenyl)-3-isopropyl-4-[(3-methyloxetan-3-yl)methoxy]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP11	J3	399	400
A195		1-(4-fluorophenyl)-3-isopropyl-4-(tetrahydrofuran-2-ylmethoxy)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP11	J3	399	400
A196		3-cyclobutyl-4-[3-(dimethylamino)propoxy]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10	J3	394	395

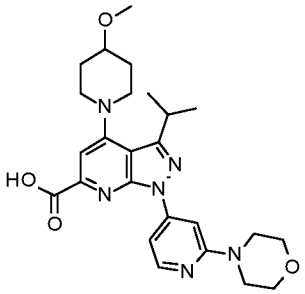
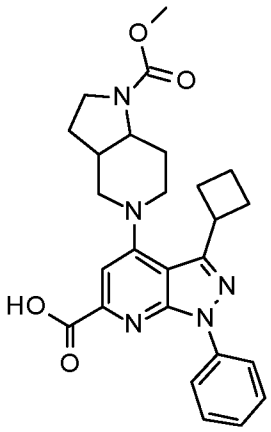
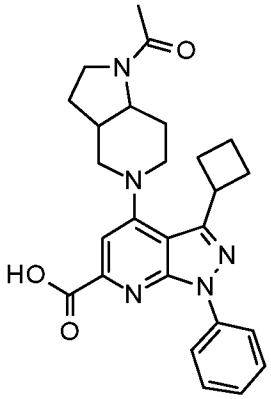
Int.	Structure	Name	SM	method	MW	Mes
A197		3-cyclobutyl-1-phenyl-4-[3-(1-piperidyl)propoxy]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10	J3	434	435
A198		4-[(3,3-difluoro-1-methyl-cyclobutyl)methoxy]-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP11	J3	433	434
A199		1-(4-fluorophenyl)-3-isopropyl-4-[3-(1-piperidyl)propoxy]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP11	J3	440	441

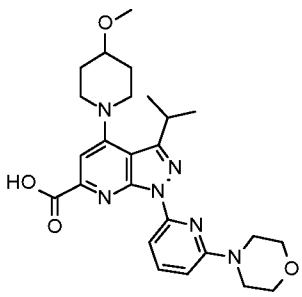
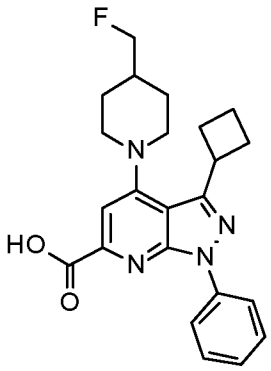
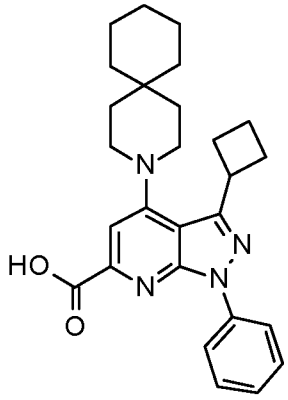
Int.	Structure	Name	SM	method	MW	Mes
A200		1-(4-fluorophenyl)-3-isopropyl-4-[2-methoxy-1-(methoxymethyl)ethoxy]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP11	J3	417	418
A201		1-(4-fluorophenyl)-4-[4-(1-hydroxy-1-methyl-ethyl)-1-piperidyl]-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E166	J1	440	441
A202		3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(methoxymethyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E167	J1	438	439

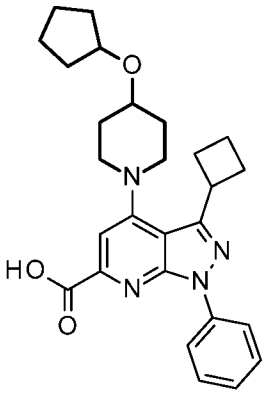
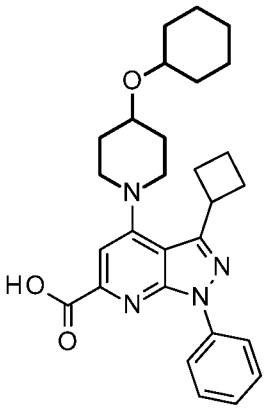
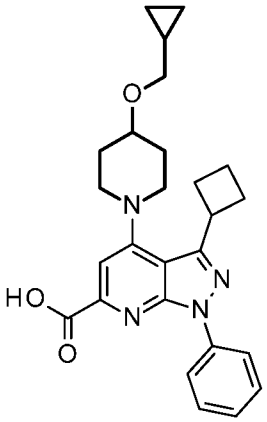
Int.	Structure	Name	SM	method	MW	Mes
A203		3-cyclobutyl-1-(4-fluorophenyl)-4-(tetrahydropyran-4-ylmethoxy)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E171	J1	425	426
A204		3-cyclobutyl-4-[4-(1-hydroxy-1-methyl-ethyl)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E170	J1	434	435
A205		4-[4-(dimethylamino)-1-piperidyl]-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E174	J1	425	426

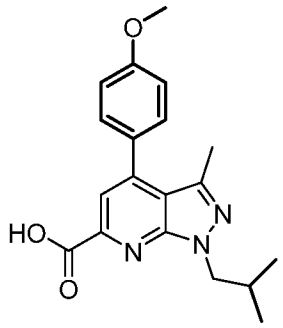
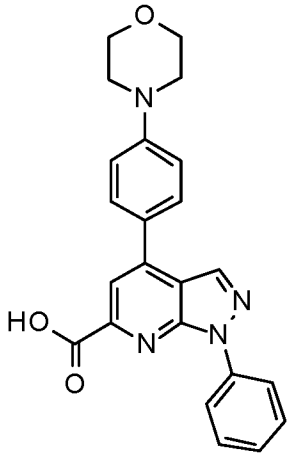
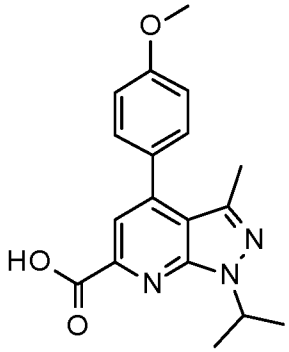
Int.	Structure	Name	SM	method	MW	Mes
A206		1-(4-fluorophenyl)-3-isopropyl-4-[4-(1-methyl-4-piperidyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E175	J1	479	480
A207		4-[(1-acetyl-4-piperidyl)methoxy]-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E176	J1	454	455
A208		1-(4-fluorophenyl)-3-isopropyl-4-[(1-methoxycarbonyl-4-piperidyl)methoxy]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E178	J1	470	471

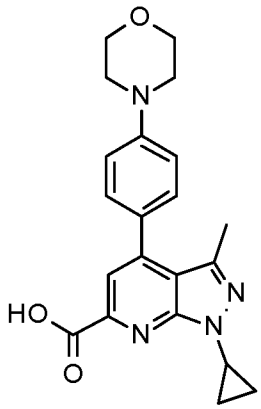
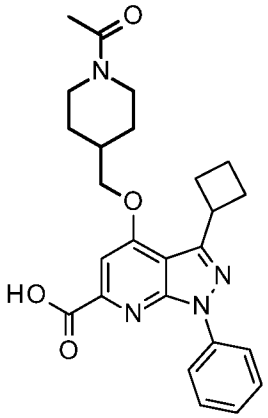
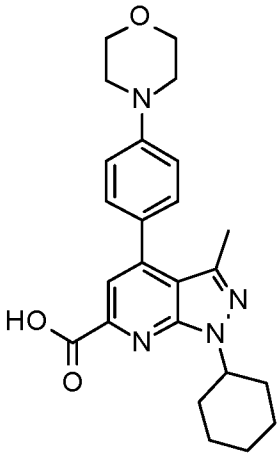
Int.	Structure	Name	SM	method	MW	Mes
A209		3-cyclobutyl-4-(1,1-dioxo-1,4-thiazinan-4-yl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E196	J1	426	427
A210		3-cyclobutyl-1-phenyl-4-(4-propoxy-1-piperidyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E078	J1	434	435
A211		3-cyclobutyl-4-(1-oxa-7-azaspiro[3.5]nonan-7-yl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E085	J1	418	419

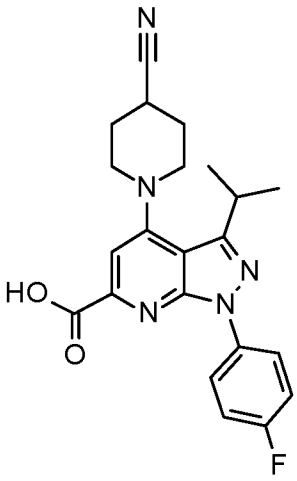
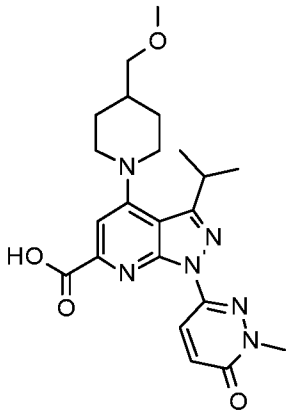
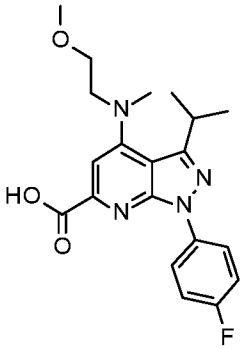
Int.	Structure	Name	SM	method	MW	Mes
A212		3-isopropyl-4-(4-methoxy-1-piperidyl)-1-(2-morpholino-4-pyridyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	A257 Specific example	J7	480	481
A213		3-cyclobutyl-4-(1-methoxycarbonyl-3,3a,4,6,7,7a-hexahydro-2*H*-pyrrolo[3,2-*c*]pyridin-5-yl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E129	J1	476	477
A214		4-(1-acetyl-3,3a,4,6,7,7a-hexahydro-2*H*-pyrrolo[3,2-*c*]pyridin-5-yl)-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E132	J1	460	461

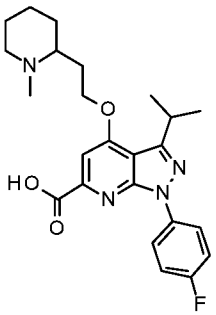
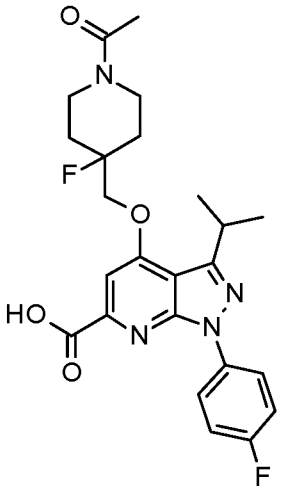
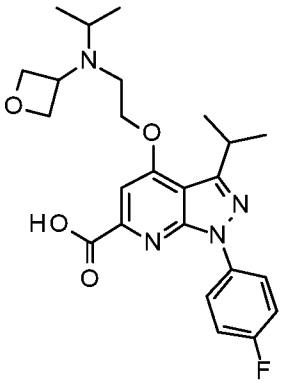
Int.	Structure	Name	SM	method	MW	Mes
A215		3-isopropyl-4-(4-methoxy-1-piperidyl)-1-(6-morpholino-2-pyridyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	A259	J7	480	481
A216		3-cyclobutyl-4-[4-(fluoromethyl)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10	J4 Specific example	408	409
A217		4-(3-azaspiro[5.5]undecan-3-yl)-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10	J4	444	445

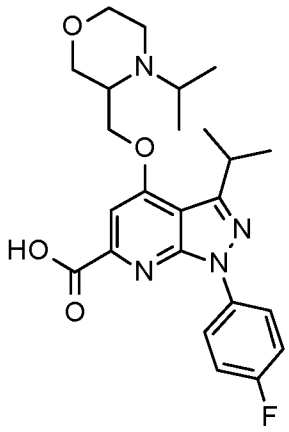
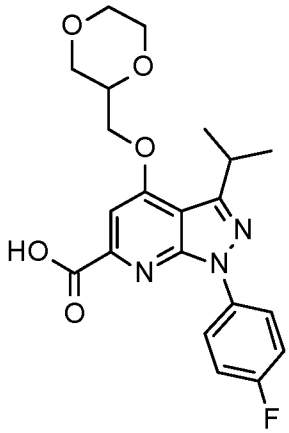
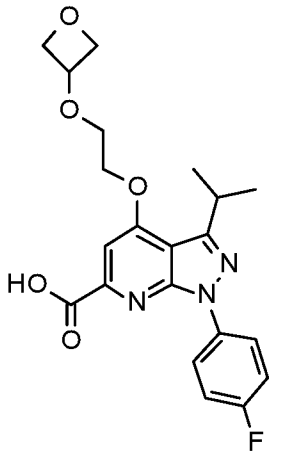
Int.	Structure	Name	SM	method	MW	Mes
A218		3-cyclobutyl-4-[4-(cyclopentoxy)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E139	J1	460	461
A219		3-cyclobutyl-4-[4-(cyclohexoxy)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E140	J1	474	475
A220		3-cyclobutyl-4-[4-(cyclopropylmethoxy)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E141	J1	446	447

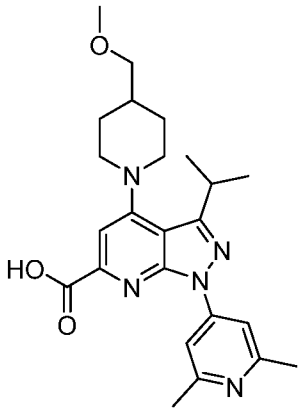
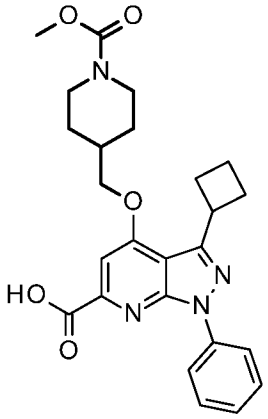
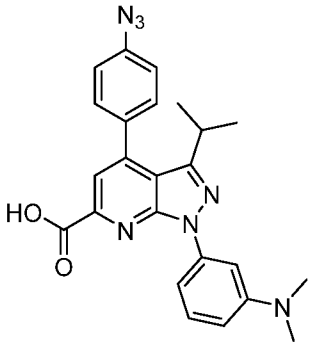
Int.	Structure	Name	SM	method	MW	Mes
A221		4-(4-methoxyphenyl)-3-methyl-1-(2-methylpropyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP06, 3524-36-5	J2	339	340
A222		4-(4-morpholinophenyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	127-17-3,1204-86-0,826-85-7	Specific example	400	401
A223		1-isopropyl-4-(4-methoxyphenyl)-3-methyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP06, 1124-16-9	J2	325	326

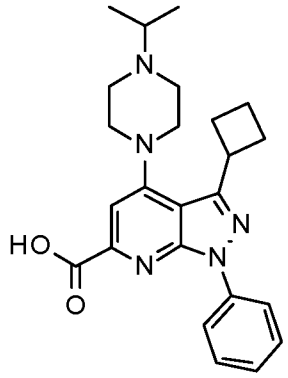
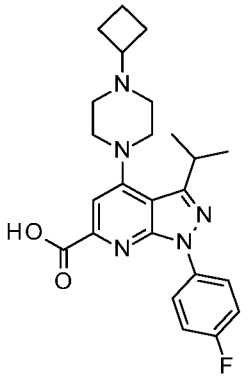
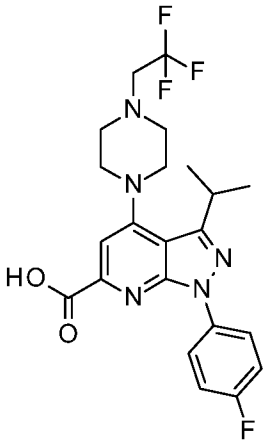
Int.	Structure	Name	SM	method	MW	Mes
A224		1-cyclopropyl-3-methyl-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP01, AMP15	J2	378	379
A225		4-[(1-acetyl-4-piperidyl)methoxy]-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	A261	J9 Specific example	448	449
A226		1-cyclohexyl-3-methyl-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP01, 56547-82-1	J2	420	421

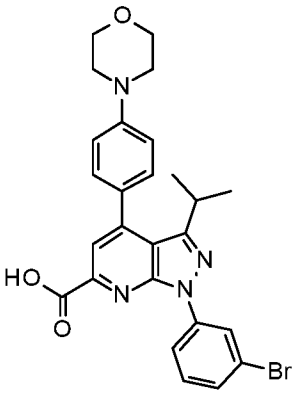
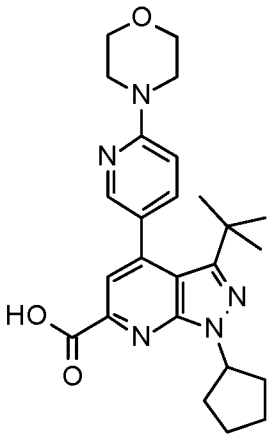
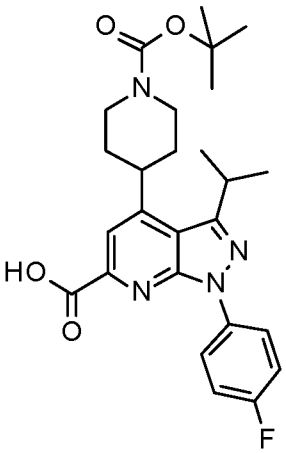
Int.	Structure	Name	SM	method	MW	Mes
A227		4-(4-cyano-1-piperidyl)-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E142	J1	407	408
A228		3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]-1-(1-methyl-6-oxo-pyridazin-3-yl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E157	J1	440	441
A229		1-(4-fluorophenyl)-3-isopropyl-4-[2-methoxyethyl(methyl)amino]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E165	J1	386	387

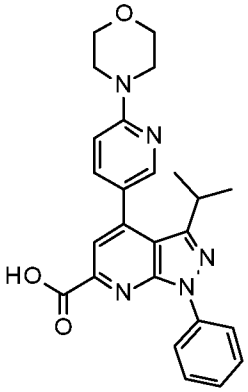
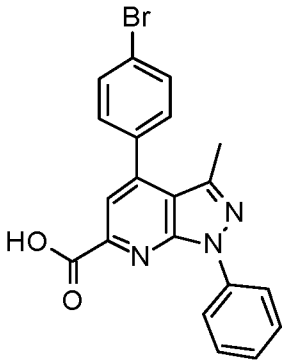
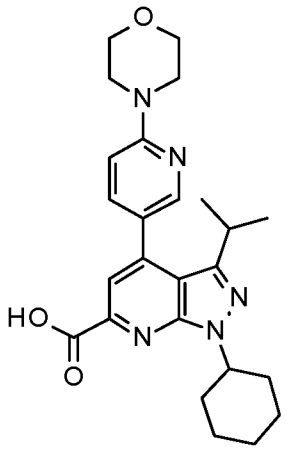
Int.	Structure	Name	SM	method	MW	Mes
A230		1-(4-fluorophenyl)-3-isopropyl-4-[2-(1-methyl-2-piperidyl)ethoxy]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP11	J3	440	441
A231		4-[(1-acetyl-4-fluoro-4-piperidyl)methoxy]-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP11, ALC03	J3	472	473
A232		1-(4-fluorophenyl)-3-isopropyl-4-[2-[isopropyl(oxetan-3-yl)amino]ethoxy]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP11, ALC04	J3	456	457

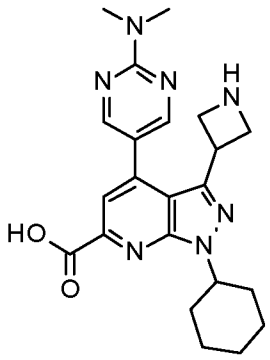
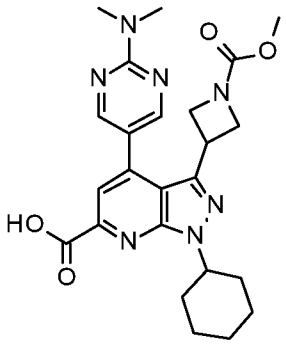
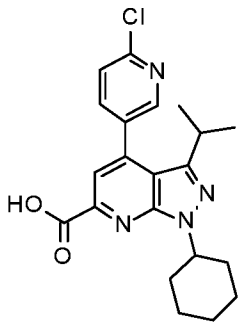
Int.	Structure	Name	SM	method	MW	Mes
A233		1-(4-fluorophenyl)-3-isopropyl-4-[(4-isopropylmorpholin-3-yl)methoxy]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP11, ALC04 (rearrangement)	J3	456	457
A234		4-(1,4-dioxan-2-ylmethoxy)-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP11, ALC05 (rearrangement)	J3	415	416
A235		1-(4-fluorophenyl)-3-isopropyl-4-[2-(oxetan-3-yloxy)ethoxy]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP11, ALC05	J3	415	416

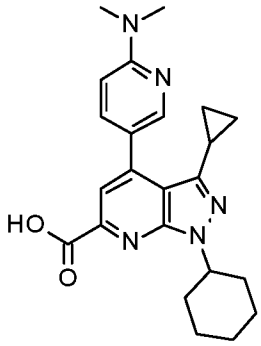
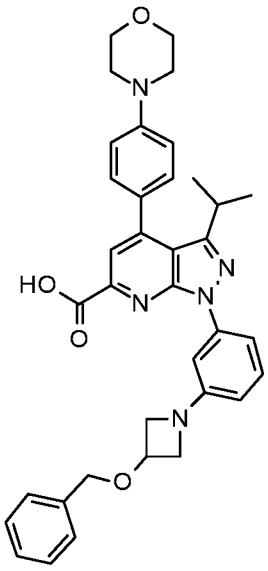
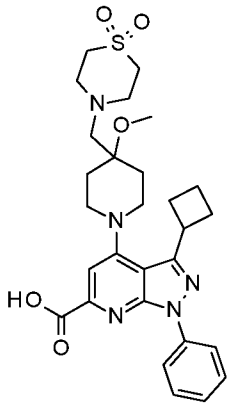
Int.	Structure	Name	SM	method	MW	Mes
A236		1-(2,6-dimethylpyridin-4-yl)-4-[4-(methoxymethyl) piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E195	J1	437	438
A237		3-cyclobutyl-4-[(1-methoxycarbonyl-4-piperidyl)methoxy]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	A261	J9 Specific example	464	465
A238		4-(4-azidophenyl)-1-[3-(dimethylamino)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E199	J1	441	442

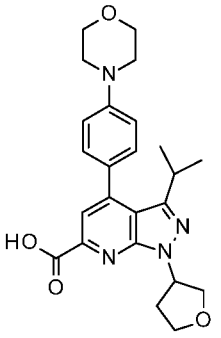
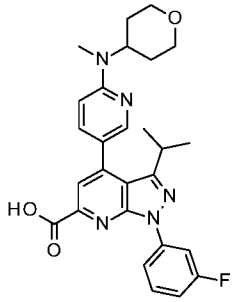
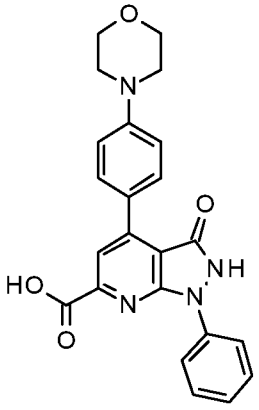
Int.	Structure	Name	SM	method	MW	Mes
A239		3-cyclobutyl-4-(4-isopropylpiperazin-1-yl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E158	J1	419	420
A240		4-(4-cyclobutylpiperazin-1-yl)-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E162	J1	437	438
A241		1-(4-fluorophenyl)-3-isopropyl-4-[4-(2,2,2-trifluoroethyl)piperazin-1-yl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E156	J1	465	466

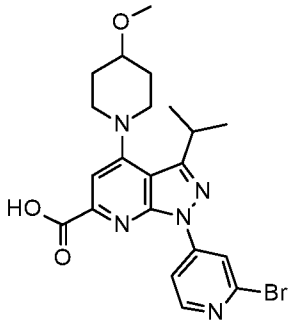
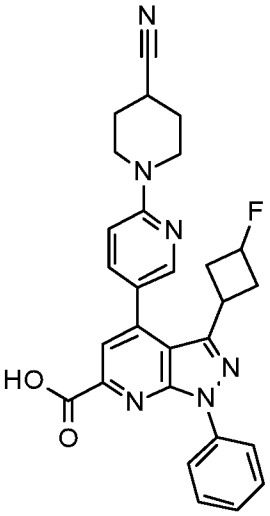
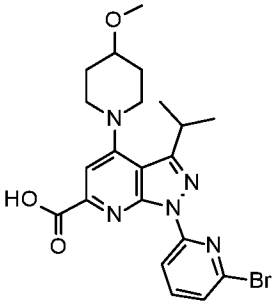
Int.	Structure	Name	SM	method	MW	Mes
A242		1-(3-bromophenyl)-3-isopropyl-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP01, AMP05	J2	520-522	521-523
A243		3-*tert*-butyl-1-cyclopentyl-4-(6-morpholino-3-pyridyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP05, AMP37	J2	449	450
A244		4-(1-*tert*-butoxycarbonyl-4-piperidyl)-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E197	J1	482	483

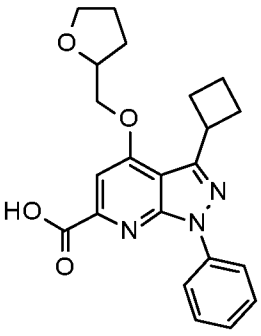
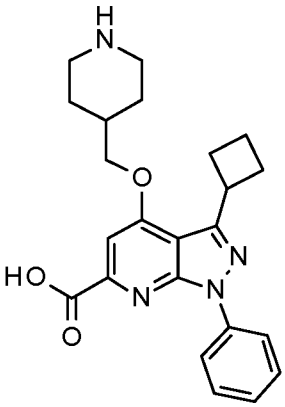
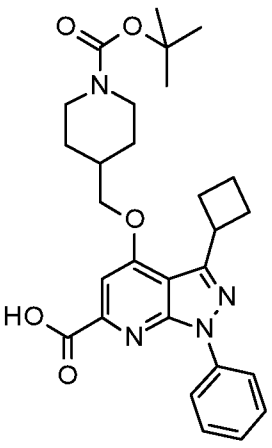
Int.	Structure	Name	SM	method	MW	Mes
A245		3-isopropyl-4-(6-morpholino-3-pyridyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E007	J1	443	444
A246		4-(4-bromophenyl)-3-methyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP19, 1131-18-6	J2	407-409	408-410
A247		1-cyclohexyl-3-isopropyl-4-(6-morpholino-3-pyridyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP05, AMP23	J2	449	450

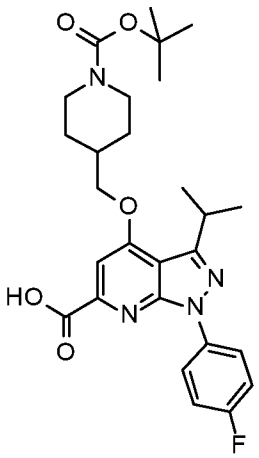
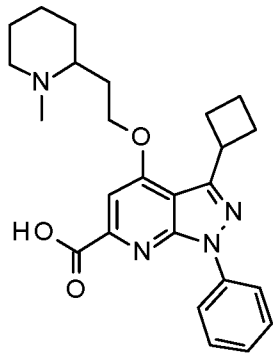
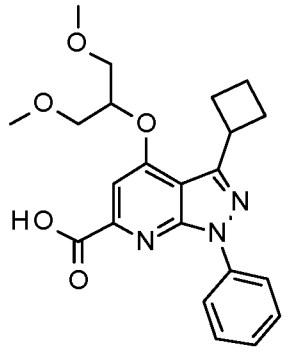
Int.	Structure	Name	SM	method	MW	Mes
A248		3-(azetidin-3-yl)-1-cyclohexyl-4-[2-(dimethylamino)pyrimidin-5-yl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP03, AMP38	J2	421	422
A249		1-cyclohexyl-4-[2-(dimethylamino)pyrimidin-5-yl]-3-(1-methoxycarbonyl azetidin-3-yl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	A248	J9 Specific example	479	480
A250		4-(6-chloro-3-pyridyl)-1-cyclohexyl-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP07, AMP23	J2	398-400	399-401

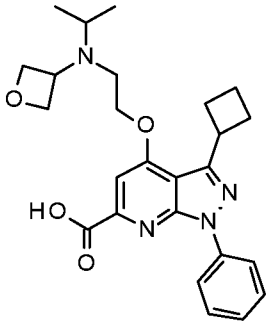
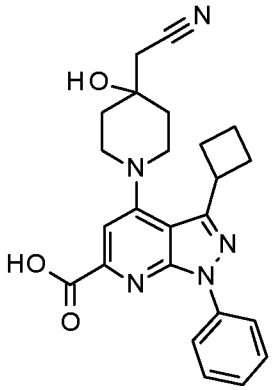
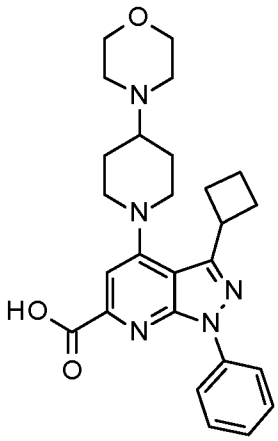
Int.	Structure	Name	SM	method	MW	Mes
A251		1-cyclohexyl-3-cyclopropyl-4-[6-(dimethylamino)-3-pyridyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E033	J1	405	406
A252		1-[3-(3-benzyloxyazetidin-1-yl)phenyl]-3-isopropyl-4-(4-morpholinophenyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	A242	J7	603	604
A253		3-cyclobutyl-4-[4-[(1,1-dioxo-1,4-thiazinan-4-yl)methyl]-4-methoxy-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E150	J8	553	554

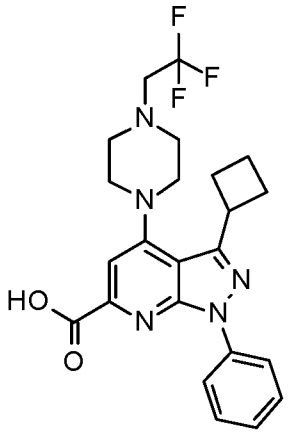
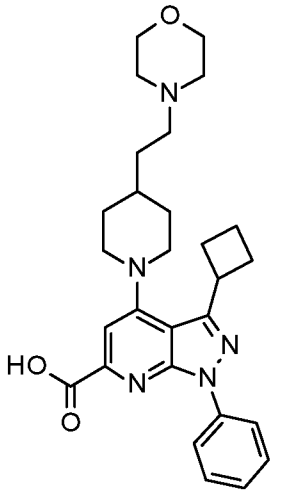
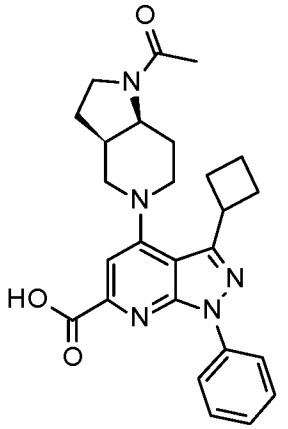
Int.	Structure	Name	SM	method	MW	Mes
A254		3-isopropyl-4-(4-morpholinophenyl)-1-tetrahydrofuran-3-yl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP01, AMP27	J2	436	437
A255		1-(3-fluorophenyl)-3-isopropyl-4-[6-[methyl(tetrahydropyran-4-yl)amino]-3-pyridyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E137	J1	489	490
A256		4-(4-morpholinophenyl)-3-oxo-1-phenyl-2*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	ALP01, 70373-98-7	J2	416	417

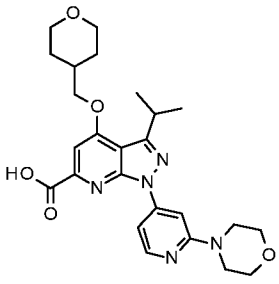
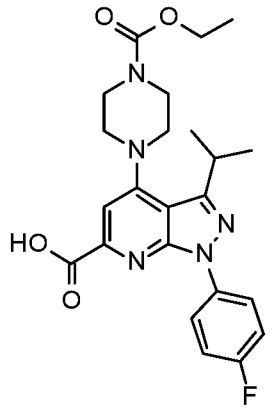
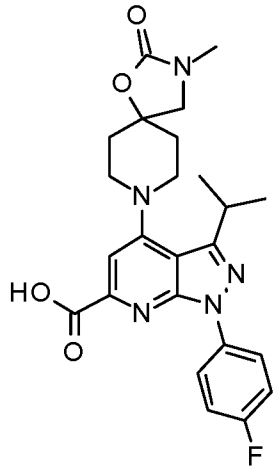
Int.	Structure	Name	SM	method	MW	Mes
A257		1-(2-bromo-4-pyridyl)-3-isopropyl-4-(4-methoxy-1-piperidyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E108	J1	473-475	474-476
A258		4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-3-(3-fluorocyclobutyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E120	J1	496	497
A259		1-(6-bromo-2-pyridyl)-3-isopropyl-4-(4-methoxy-1-piperidyl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E133	J1	473-475	474-476

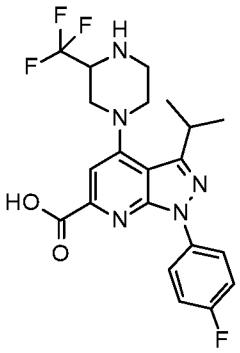
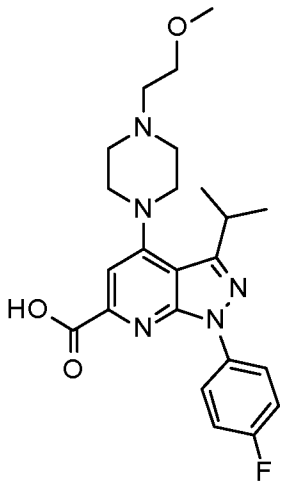
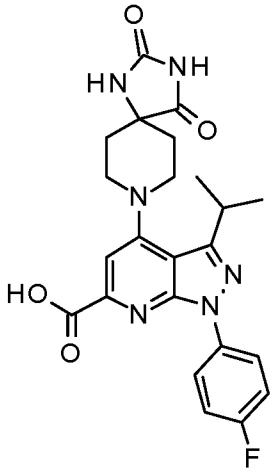
Int.	Structure	Name	SM	method	MW	Mes
A260		3-cyclobutyl-1-phenyl-4-(tetrahydrofuran-2-ylmethoxy)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10	J3	393	394
A261		3-cyclobutyl-1-phenyl-4-(4-piperidylmethoxy)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	A262	I25	406	407
A262		4-[(1-*tert*-butoxycarbonyl-4-piperidyl)methoxy]-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10	J3	506	507

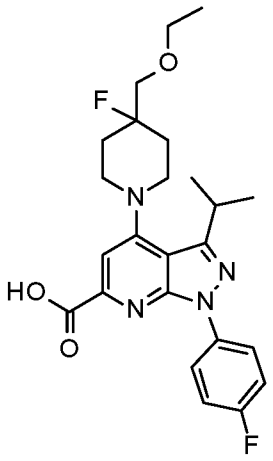
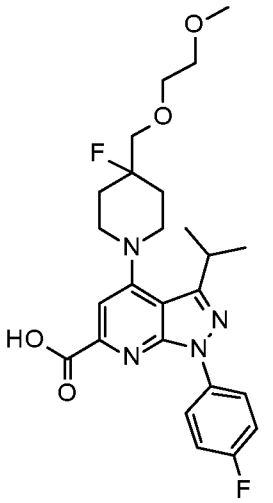
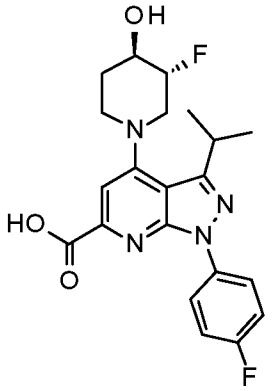
Int.	Structure	Name	SM	method	MW	Mes
A263		4-[(1-*tert*-butoxycarbonyl-4-piperidyl)methoxy]-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP11	J3	512	513
A264		3-cyclobutyl-4-[2-(1-methyl-2-piperidyl)ethoxy]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10	J3	434	435
A265		3-cyclobutyl-4-[2-methoxy-1-(methoxymethyl)ethoxy]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10	J3	411	412

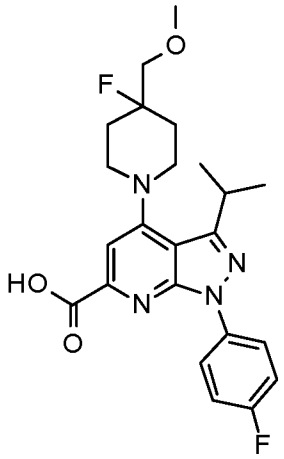
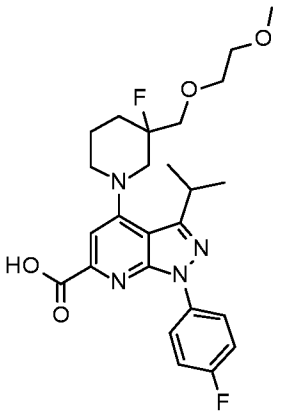
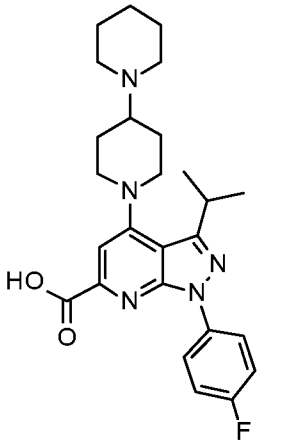
Int.	Structure	Name	SM	method	MW	Mes
A266		3-cyclobutyl-4-[2-[isopropyl(oxetan-3-yl)amino]ethoxy]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10	J3	450	451
A267		4-[4-(cyanomethyl)-4-hydroxy-1-piperidyl]-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E179	J1	431	432
A268		3-cyclobutyl-4-(4-morpholino-1-piperidyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10	J10 Specific example	461	462

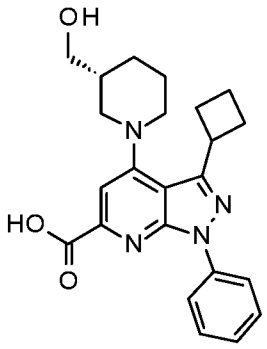
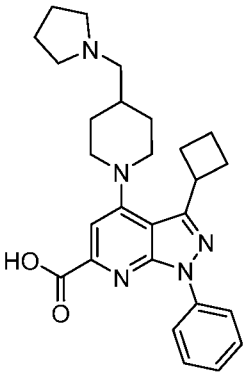
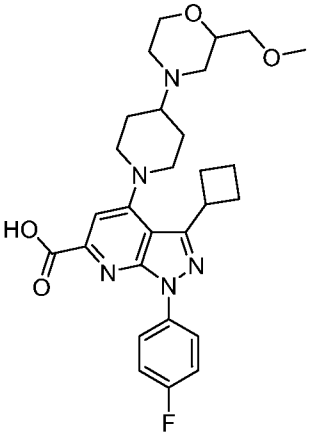
Int.	Structure	Name	SM	method	MW	Mes
A269		3-cyclobutyl-1-phenyl-4-[4-(2,2,2-trifluoroethyl)piperazin-1-yl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E180	J1	459	460
A270		3-cyclobutyl-4-[4-(2-morpholinoethyl)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10	J10 Specific example	489	490
A271		4-[(3aR,7aS)-1-acetyl-3,3a,4,6,7,7a-hexahydro-2*H*-pyrrolo[3,2-*c*]pyridin-5-yl]-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10	J10, I25, J9 Specific example	459	458 (ESI-)

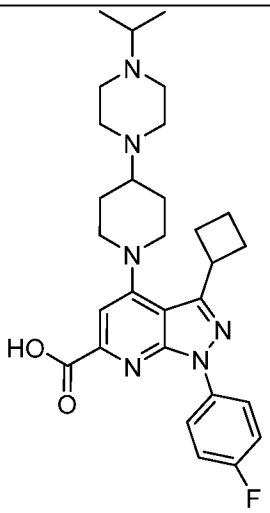
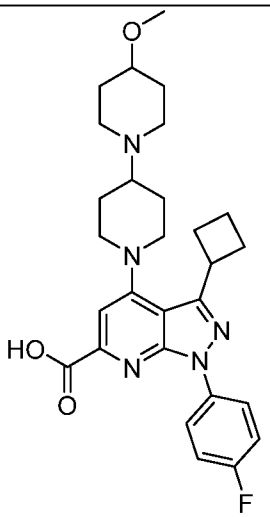
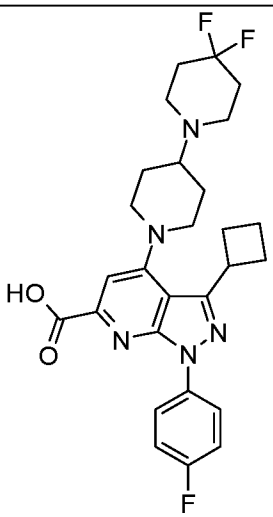
Int.	Structure	Name	SM	method	MW	Mes
A272		3-isopropyl-1-(2-morpholino-4-pyridyl)-4-(tetrahydropyran-4-ylmethoxy)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E181	J6	481	482
A273		4-(4-ethoxycarbonylpiperazin-1-yl)-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E184	J1	455	456
A274		1-(4-fluorophenyl)-3-isopropyl-4-(3-methyl-2-oxo-1-oxa-3,8-diazaspiro[4.5]decan-8-yl)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E185	J1	467	468

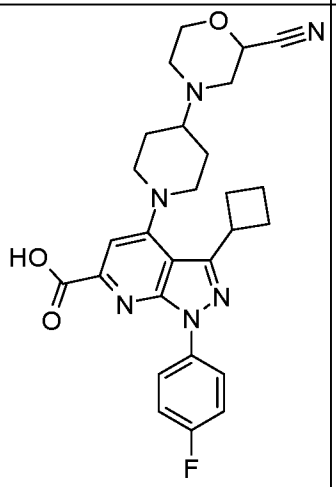
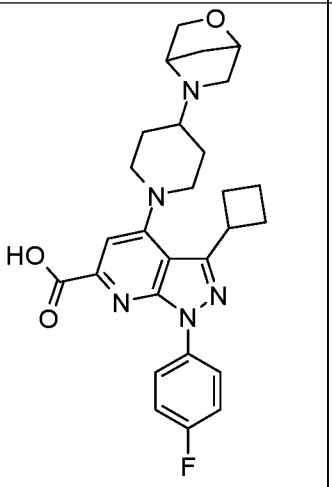
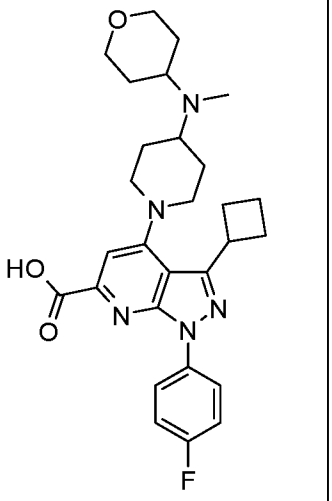
Int.	Structure	Name	SM	method	MW	Mes
A275		1-(4-fluorophenyl)-3-isopropyl-4-[3-(trifluoromethyl)piperazin-1-yl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E186	J1	451	452
A276		1-(4-fluorophenyl)-3-isopropyl-4-[4-(2-methoxyethyl)piperazin-1-yl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E187	J1	441	442
A277		4-(2,4-dioxo-1,3,8-triazaspiro[4.5]decan-8-yl)-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E188	J1	466	467

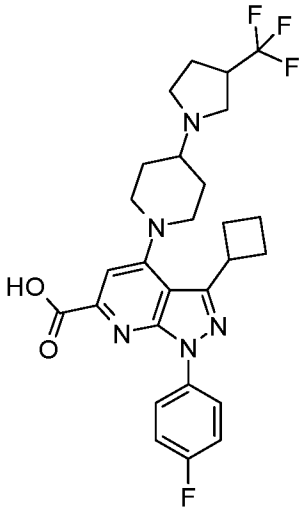
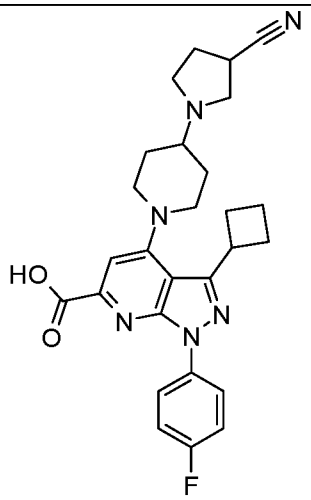
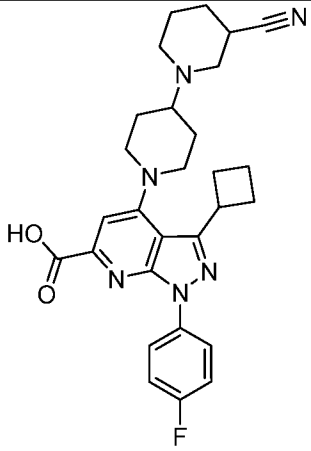
Int.	Structure	Name	SM	method	MW	Mes
A278		4-[4-(ethoxymethyl)-4-fluoro-1-piperidyl]-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E189	J1	458	459
A279		4-[4-fluoro-4-(2-methoxyethoxymethyl)-1-piperidyl]-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E190	J1	488	489
A280		4-[(3R,4R)-3-fluoro-4-hydroxy-1-piperidyl]-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E191	J1	416	417

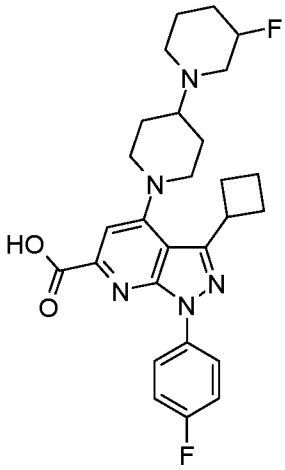
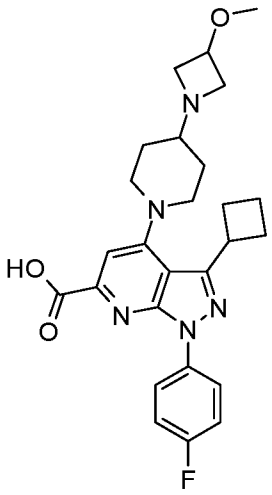
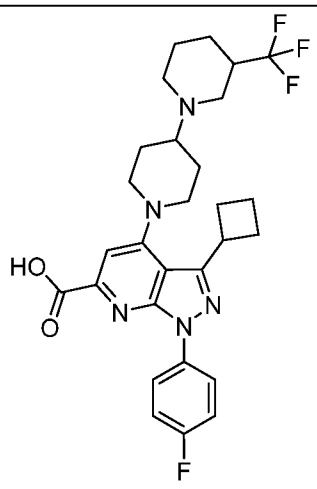
Int.	Structure	Name	SM	method	MW	Mes
A281		4-[4-fluoro-4-(methoxymethyl)-1-piperidyl]-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E192	J1	444	445
A282		4-[3-fluoro-3-(2-methoxyethoxymethyl)-1-piperidyl]-1-(4-fluorophenyl)-3-isopropyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E193	J1	488	489
A283		1-(4-fluorophenyl)-3-isopropyl-4-[4-(1-piperidyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E194	J1	465	466

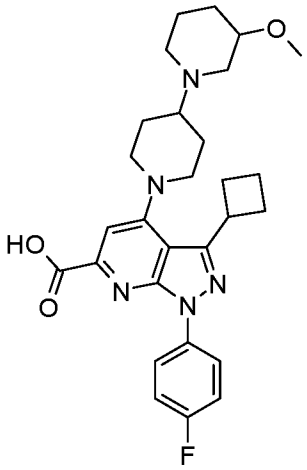
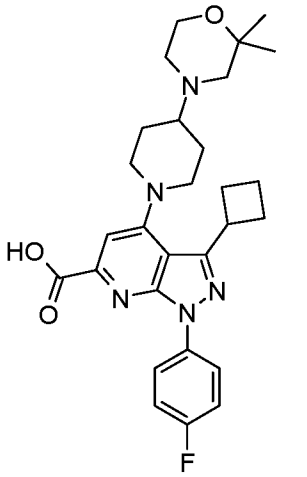
Int.	Structure	Name	SM	method	MW	Mes
A284		3-cyclobutyl-4-[(3R)-3-(hydroxymethyl)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10	J10 Specific example	406	407
A285		3-cyclobutyl-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E357	J1, Specific example	459	460
A286		3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[2-(methoxymethyl) morpholin-4-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E354	J1	523	523

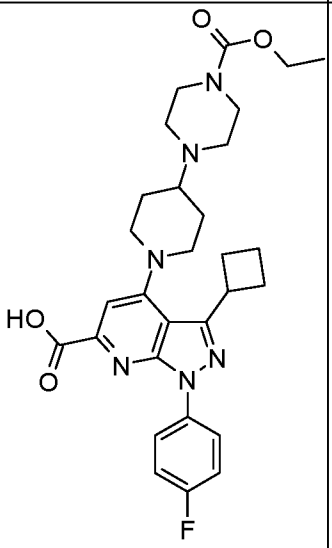
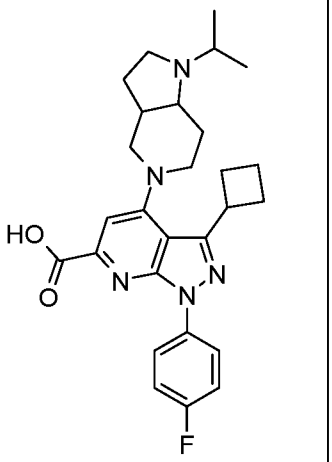
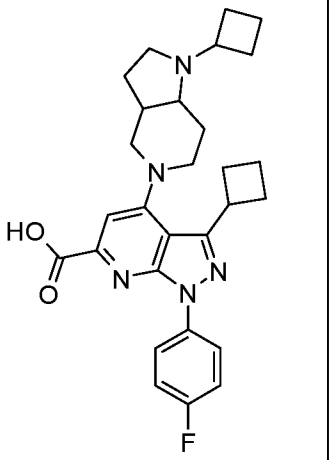
Int.	Structure	Name	SM	method	MW	Mes
A287		3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[4-(propan-2-yl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E355	J1	520	521
A288		3-cyclobutyl-1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E356	J1	507	508
A289		3-cyclobutyl-4-(4,4-difluoro[1,4'-bipiperidin]-1'-yl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E358	J1	513	514

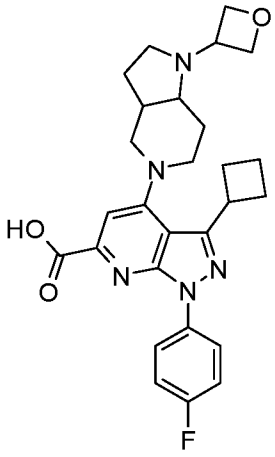
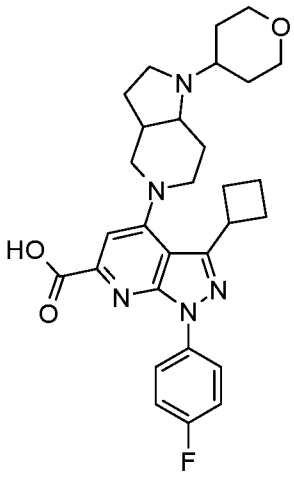
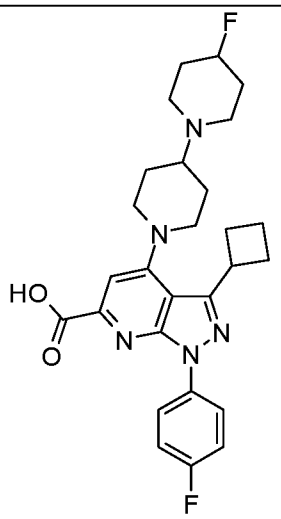
Int.	Structure	Name	SM	method	MW	Mes
A290		4-[4-(2-cyanomorpholin-4-yl)piperidin-1-yl]-3-cyclobutyl-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E359	J1	504	505
A291		3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E360	J1	491	492
A292		3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[methyl(oxan-4-yl)amino]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E361	J1	507	508

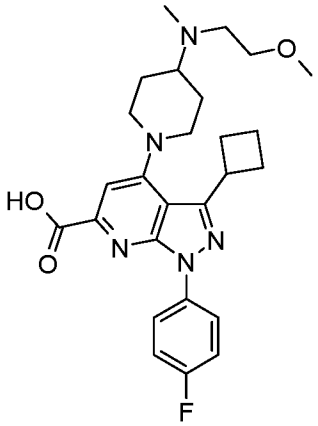
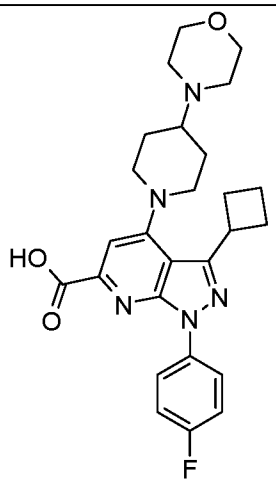
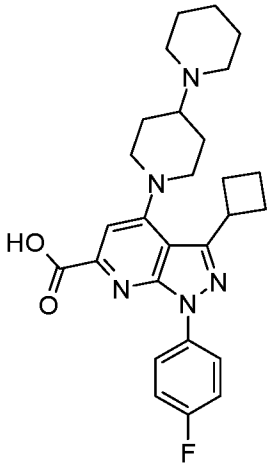
Int.	Structure	Name	SM	method	MW	Mes
A293		3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[3-(trifluoromethyl)pyrrolidin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E362	J1	531	532
A294		4-[4-(3-cyanopyrrolidin-1-yl)piperidin-1-yl]-3-cyclobutyl-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E363	J1	488	489
A295		4-(3-cyano[1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E364	J1	502	503

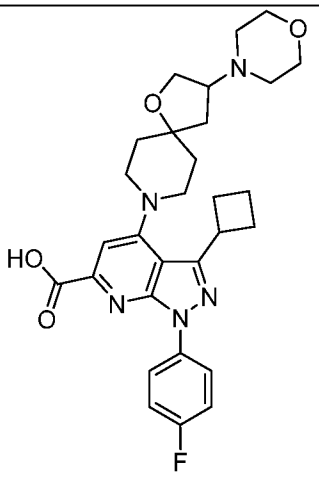
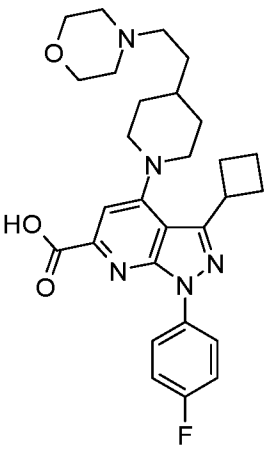
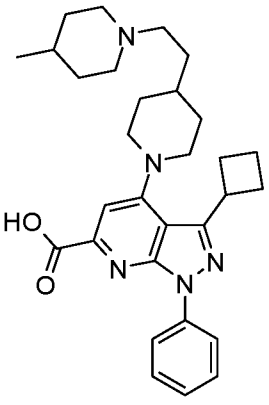
Int.	Structure	Name	SM	method	MW	Mes
A296		3-cyclobutyl-4-(3-fluoro[1,4'-bipiperidin]-1'-yl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E365	J1	495	496
A297		3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(3-methoxyazetidin-1-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E366	J1A	479	480
A298		3-cyclobutyl-1-(4-fluorophenyl)-4-[3-(trifluoromethyl)[1,4'-bipiperidin]-1'-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E367	J1A	545	546

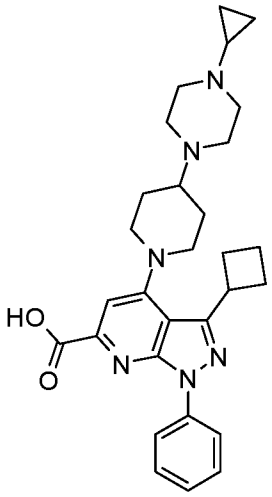
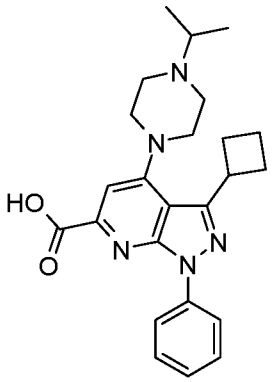
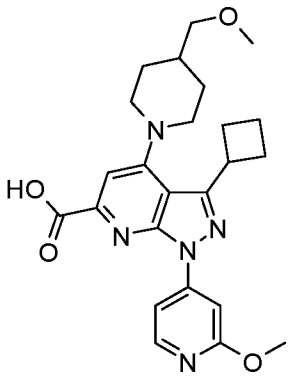
Int.	Structure	Name	SM	method	MW	Mes
A299		3-cyclobutyl-1-(4-fluorophenyl)-4-(3-methoxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E368	J1A	507	508
A300		3-cyclobutyl-4-[4-(2,2-dimethylmorpholin-4-yl)piperidin-1-yl]-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E369	J1A	507	508

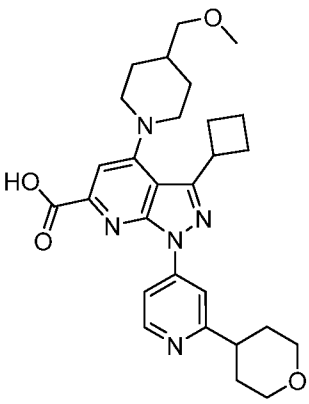
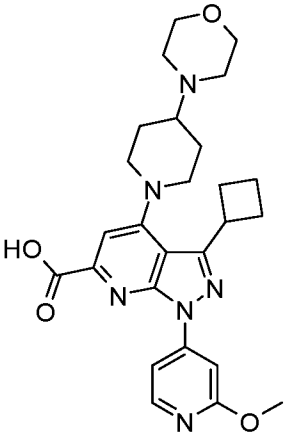
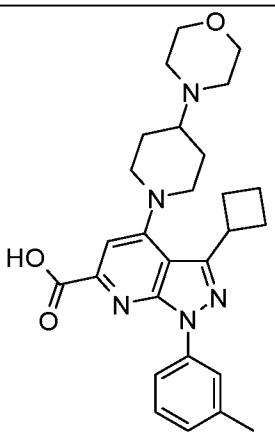
Int.	Structure	Name	SM	method	MW	Mes
A301		3-cyclobutyl-4-{4-[4-(ethoxycarbonyl)piperazin-1-yl]piperidin-1-yl}-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E370	J1A	550	551
A302		3-cyclobutyl-1-(4-fluorophenyl)-4-[1-(propan-2-yl)octahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E371	J1	477	478
A303		3-cyclobutyl-4-(1-cyclobutyloctahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E372	J1	489	490

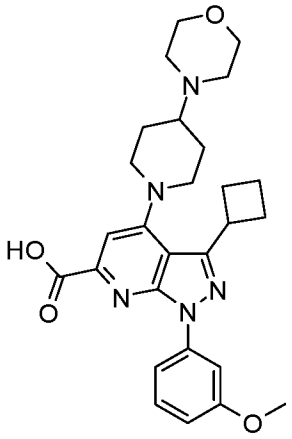
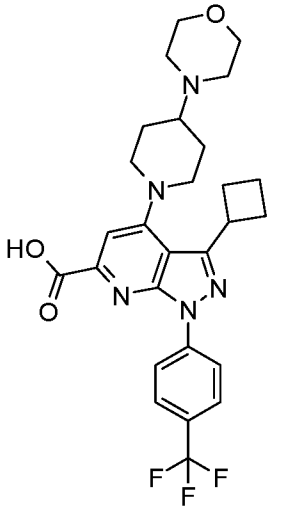
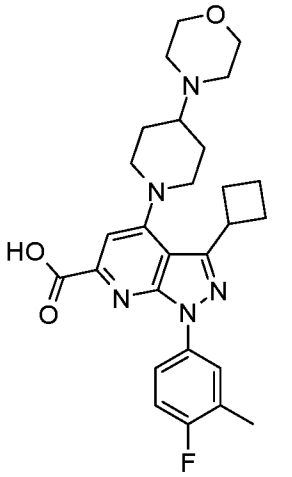
Int.	Structure	Name	SM	method	MW	Mes
A304		3-cyclobutyl-1-(4-fluorophenyl)-4-[1-(oxetan-3-yl)octahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E373	J1	491	492
A305		3-cyclobutyl-1-(4-fluorophenyl)-4-[1-(oxan-4-yl)octahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E374	J1	519	520
A306		3-cyclobutyl-4-(4-fluoro[1,4'-bipiperidin]-1'-yl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E375	J1	495	496

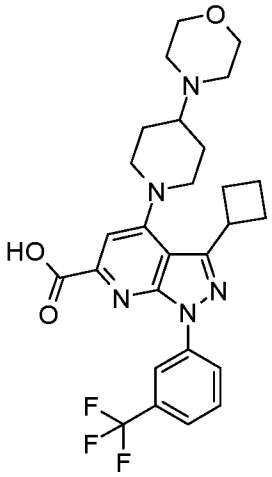
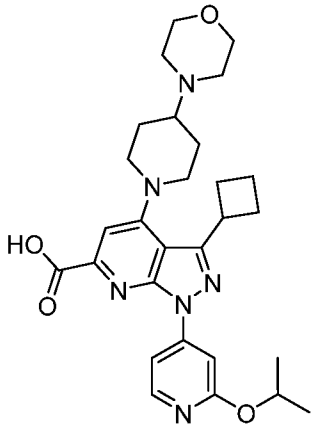
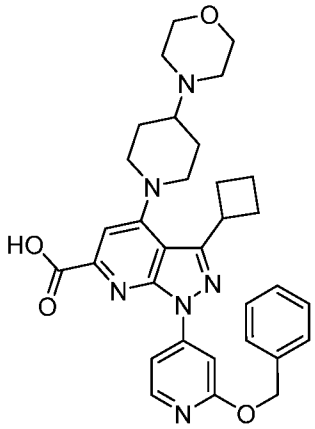
Int.	Structure	Name	SM	method	MW	Mes
A307		3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[(2-methoxyethyl)(methyl)amino]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E376	J1A	481	482
A308		3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E377	J1	479	480
A309		4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E378	J1	477	478

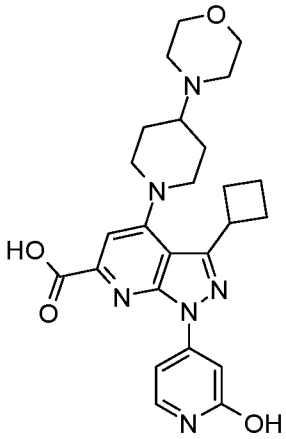
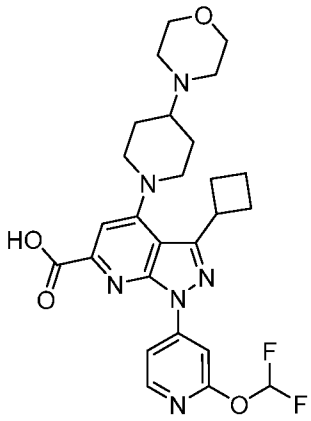
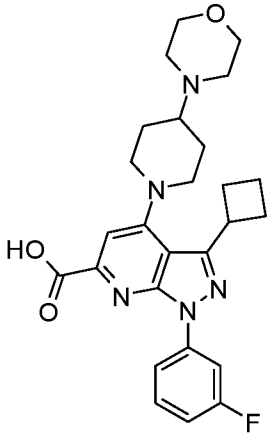
Int.	Structure	Name	SM	method	MW	Mes
A310		3-cyclobutyl-1-(4-fluorophenyl)-4-[3-(morpholin-4-yl)-1-oxa-8-azaspiro[4.5]decan-8-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E381	J1	535	536
A311		3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[2-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E382	J1	507	508
A312		3-cyclobutyl-4-{4-[2-(4-methylpiperidin-1-yl)ethyl]piperidin-1-yl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E383	J1	501	502

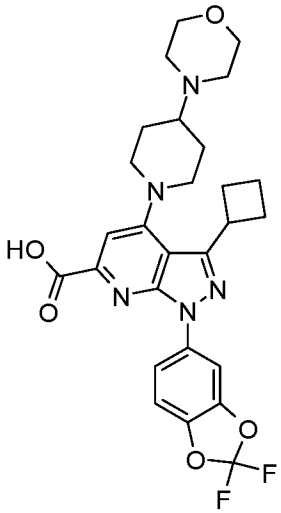
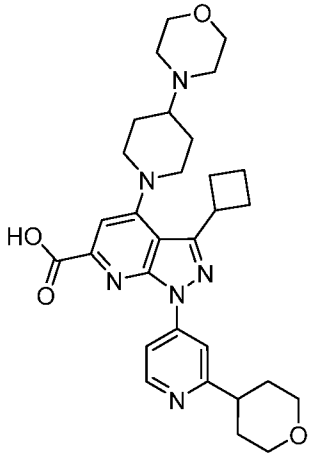
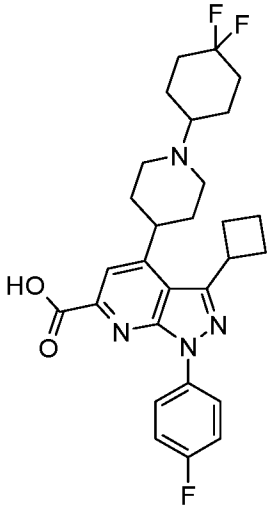
Int.	Structure	Name	SM	method	MW	Mes
A313		3-cyclobutyl-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E384	J1	500	501
A314		3-cyclobutyl-1-phenyl-4-[4-(propan-2-yl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E385	J1	419	420
A315		3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-(2-methoxypyridin-4-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E388	J1	451	452

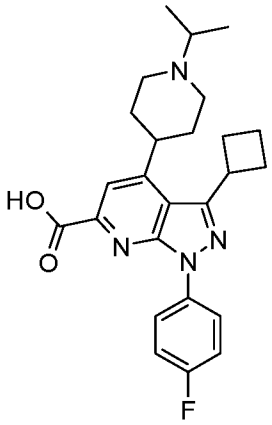
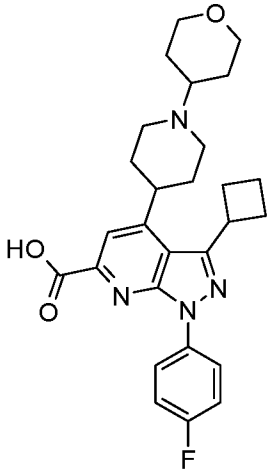
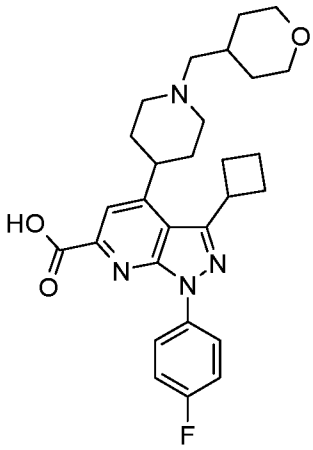
Int.	Structure	Name	SM	method	MW	Mes
A316		3-cyclobutyl-4-[4-(methoxymethyl) piperidin-1-yl]-1-[2-(oxan-4-yl)pyridin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E391	J1A	505	506
A317		3-cyclobutyl-1-(2-methoxypyridin-4-yl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E394	J1A	492	493
A318a		3-cyclobutyl-1-(3-methylphenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E395	J1A Specific example	475	476

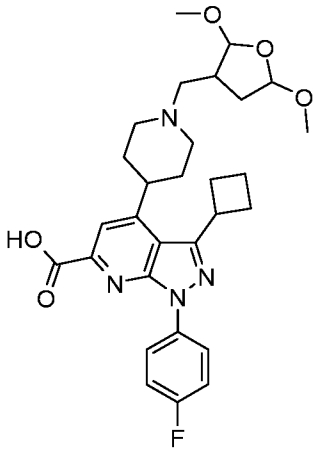
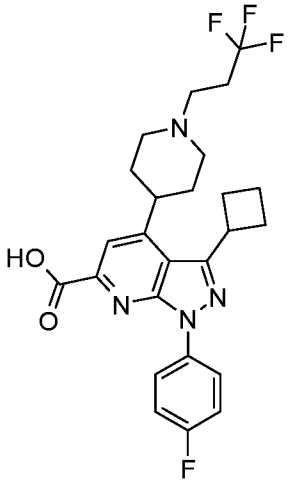
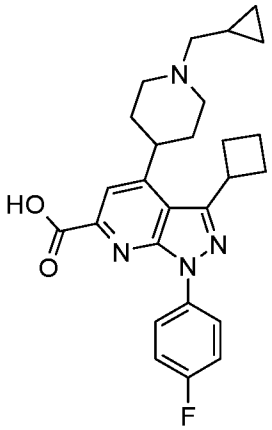
Int.	Structure	Name	SM	method	MW	Mes
A318b		3-cyclobutyl-1-(3-methoxyphenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E396	J1A	491	492
A319		3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-[4-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E397	J1A	529	530
A320		3-cyclobutyl-1-(4-fluoro-3-methylphenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E398	J1A	493	494

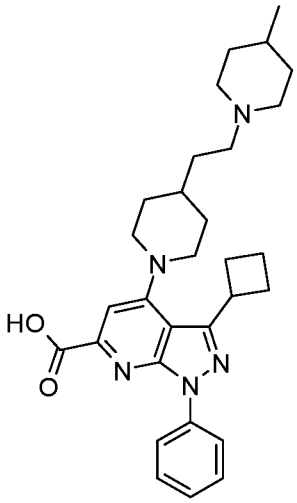
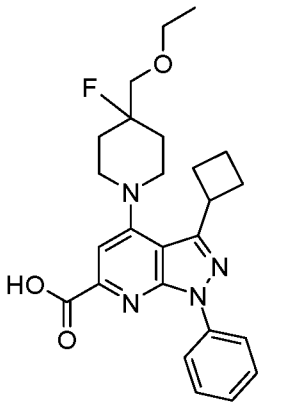
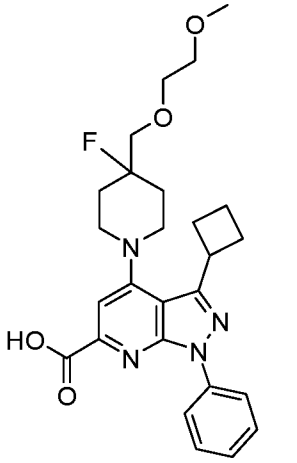
Int.	Structure	Name	SM	method	MW	Mes
A321		3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E399	J1A	529	530
A322		3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-{2-[(propan-2-yl)oxy]pyridin-4-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E400	J1A	520	521
A323		1-[2-(benzyloxy)pyridin-4-yl]-3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E401	J1A	568	569

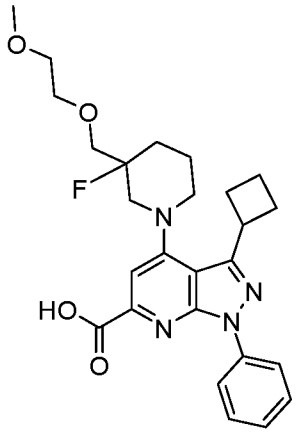
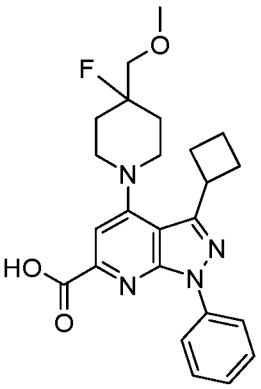
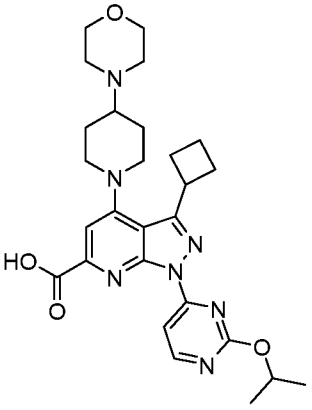
Int.	Structure	Name	SM	method	MW	Mes
A324		3-cyclobutyl-1-(2-hydroxypyridin-4-yl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E402	J1A	478	479
A325		3-cyclobutyl-1-[2-(difluoromethoxy)pyridin-4-yl]-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E403	J1A	528	529
A326		3-cyclobutyl-1-(3-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E404	J1A	479	480

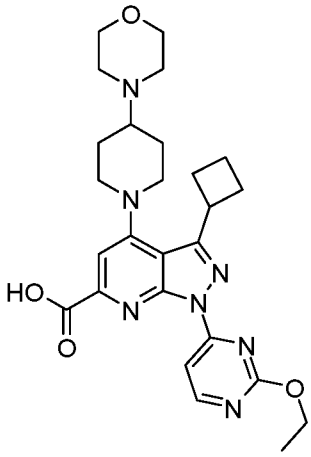
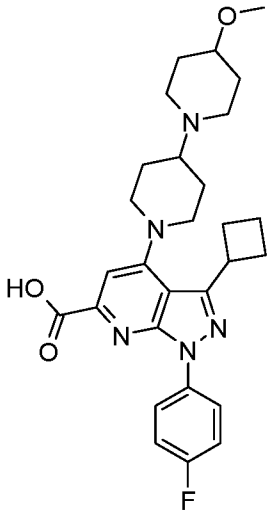
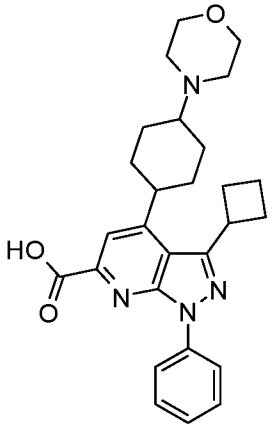
Int.	Structure	Name	SM	method	MW	Mes
A327		3-cyclobutyl-1-(2,2-difluoro-2*H*-1,3-benzodioxol-5-yl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E405	J1A	541	542
A328		3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-[2-(oxan-4-yl)pyridin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E407	J1A	546	547
A329		3-cyclobutyl-4-[1-(4,4-difluorocyclohexyl)piperidin-4-yl]-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E414	J1A	512	513

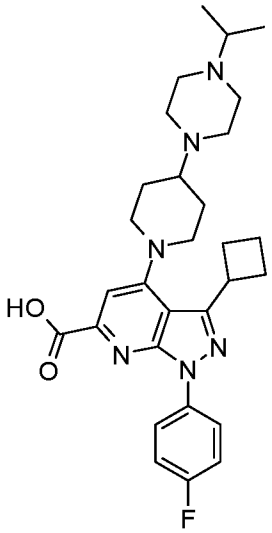
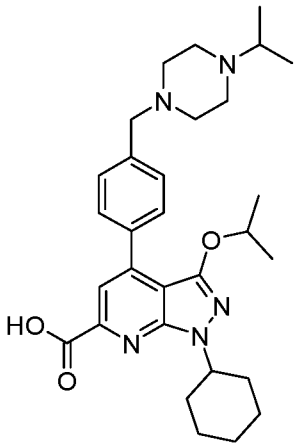
Int.	Structure	Name	SM	method	MW	Mes
A330		3-cyclobutyl-1-(4-fluorophenyl)-4-[1-(propan-2-yl)piperidin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E415	J1A	436	437
A331		3-cyclobutyl-1-(4-fluorophenyl)-4-[1-(oxan-4-yl)piperidin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E416	J1A	478	479
A332		3-cyclobutyl-1-(4-fluorophenyl)-4-{1-[(oxan-4-yl)methyl]piperidin-4-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E417	J1A	492	493

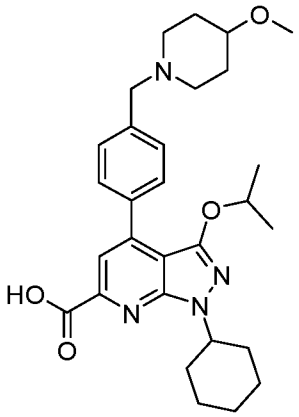
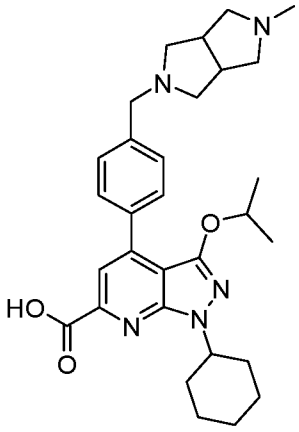
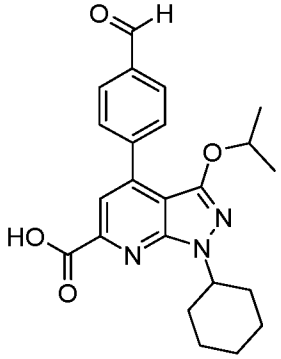
Int.	Structure	Name	SM	method	MW	Mes
A333		3-cyclobutyl-4-{1-[(2,5-dimethoxyoxolan-3-yl)methyl]piperidin-4-yl}-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E418	J1A	538	539
A334		3-cyclobutyl-1-(4-fluorophenyl)-4-[1-(3,3,3-trifluoropropyl)piperidin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E419	J1A	490	491
A336		3-cyclobutyl-4-[1-(cyclopropylmethyl)piperidin-4-yl]-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E421	J1A	448	449

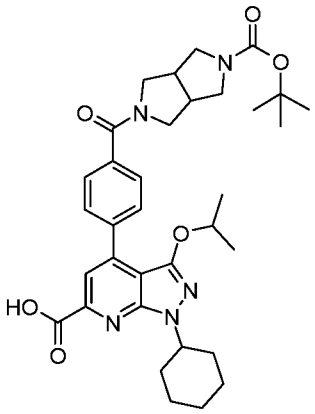
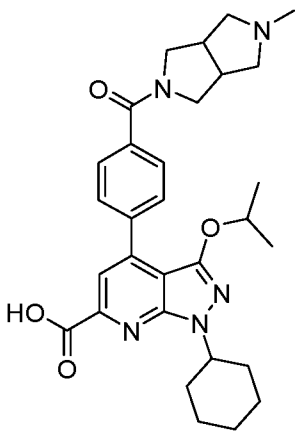
Int.	Structure	Name	SM	method	MW	Mes
A337		3-cyclobutyl-4-{4-[2-(4-methylpiperidin-1-yl)ethyl]piperidin-1-yl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E412	J1A	501	502
A338		3-cyclobutyl-4-[4-(ethoxymethyl)-4-fluoropiperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E408	J1	452	453
A339		3-cyclobutyl-4-{4-fluoro-4-[(2-methoxyethoxy)methyl]piperidin-1-yl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E409	J1	482	483

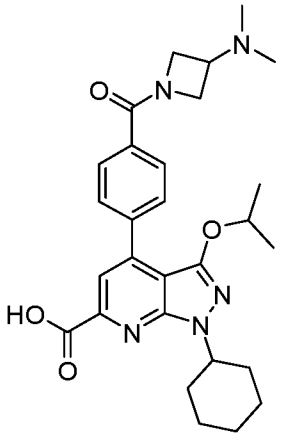
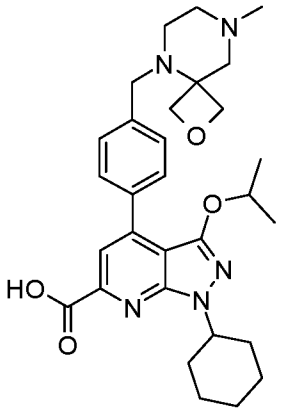
Int.	Structure	Name	SM	method	MW	Mes
A340		3-cyclobutyl-4-{3-fluoro-3-[(2-methoxyethoxy)methyl]piperidin-1-yl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E410	J1	482	483
A341		3-cyclobutyl-4-[4-fluoro-4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E411	J1	438	439
A342		3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-{2-[(propan-2-yl)oxy]pyrimidin-4-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E422	J11	521	522

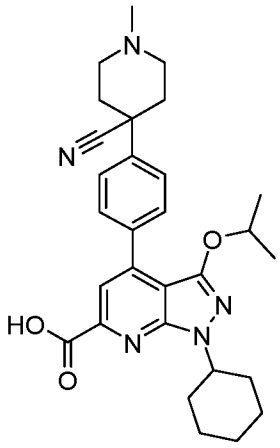
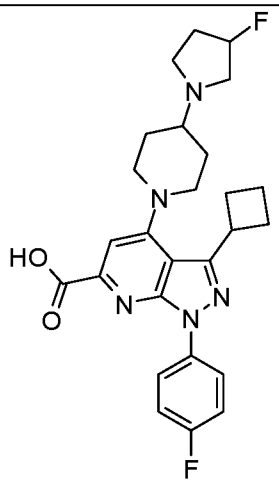
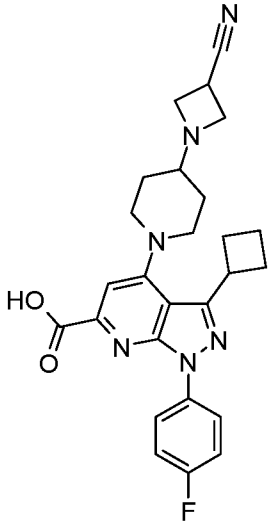
Int.	Structure	Name	SM	method	MW	Mes
A343		3-cyclobutyl-1-(2-ethoxypyrimidin-4-yl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E422	J11 Specific example	507	508
A344		3-cyclobutyl-1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E424	J1A	507	508
A345		3-cyclobutyl-4-[4-(morpholin-4-yl)cyclohexyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E433	J1A	460	461

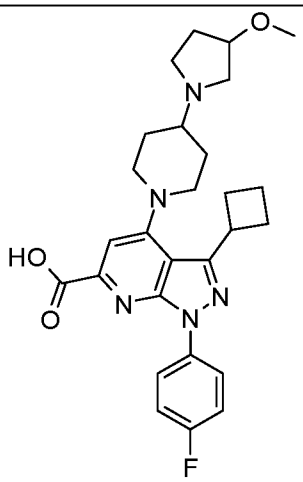
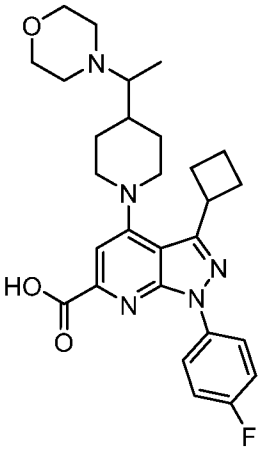
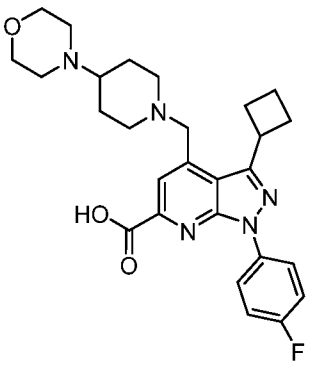
Int.	Structure	Name	SM	method	MW	Mes
A346		3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[4-(propan-2-yl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E434	J1	520	521
A347		1-cyclohexyl-3-[(propan-2-yl)oxy]-4-(4-{[4-(propan-2-yl)piperazin-1-yl]methyl}phenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E435	J1	519	520

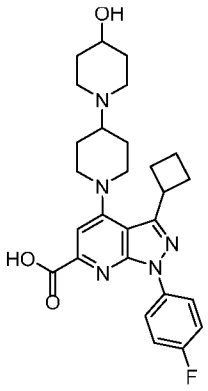
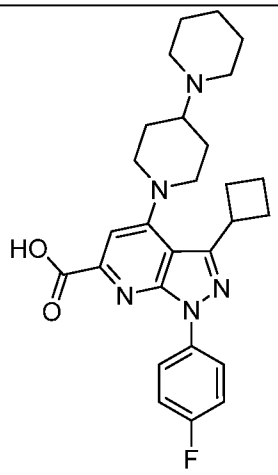
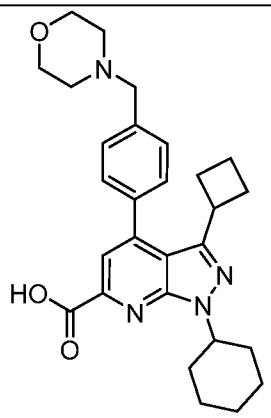
Int.	Structure	Name	SM	method	MW	Mes
A348		1-cyclohexyl-4-{4-[(4-methoxypiperidin-1-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E436	J1	506	507
A349		1-cyclohexyl-4-{4-[(5-methylhexahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E437	J1	517	518
A350		1-cyclohexyl-4-(4-formylphenyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E425	J1	407	408

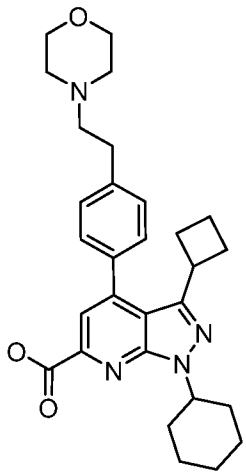
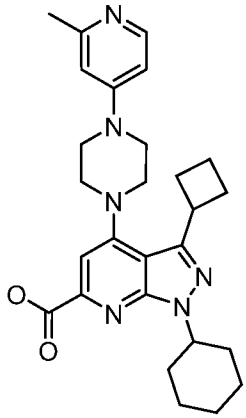
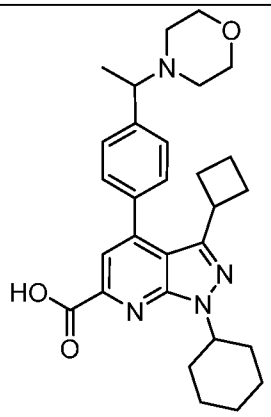
Int.	Structure	Name	SM	method	MW	Mes
A351		4-{4-[5-(*tert*-butoxycarbonyl)hexahydropyrrolo[3,4-*c*]pyrrole-2(1*H*)-carbonyl]phenyl}-1-cyclohexyl-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E439	J1A	617	618
A352		1-cyclohexyl-4-[4-(5-methylhexahydropyrrolo[3,4-*c*]pyrrole-2(1*H*)-carbonyl)phenyl]-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E440	J1A	531	532

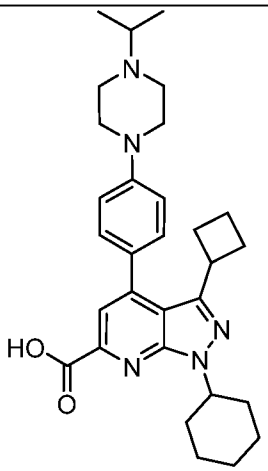
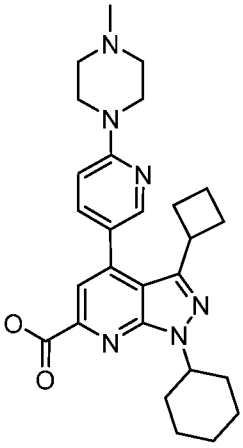
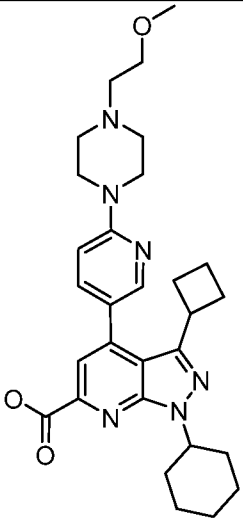
Int.	Structure	Name	SM	method	MW	Mes
A353		1-cyclohexyl-4-{4-[3-(dimethylamino)azetidine-1-carbonyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E441	J1A	505	506
A354		1-cyclohexyl-4-{4-[(8-methyl-2-oxa-5,8-diazaspiro[3.5]nonan-5-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E444	J1A	533	534

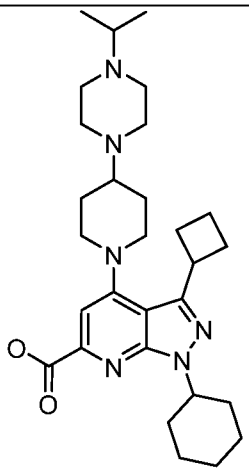
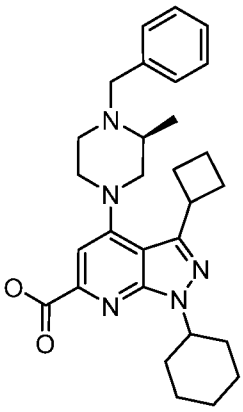
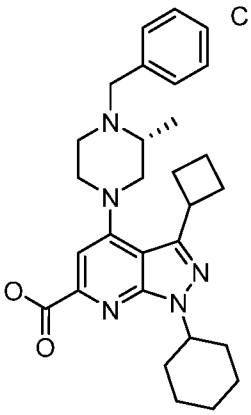
Int.	Structure	Name	SM	method	MW	Mes
A355		4-[4-(4-cyano-1-methylpiperidin-4-yl)phenyl]-1-cyclohexyl-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E445	J1A	501	502
A356		3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(3-fluoropyrrolidin-1-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E427	J1	481	482
A357		4-[4-(3-cyanoazetidin-1-yl)piperidin-1-yl]-3-cyclobutyl-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E428	J1	474	475

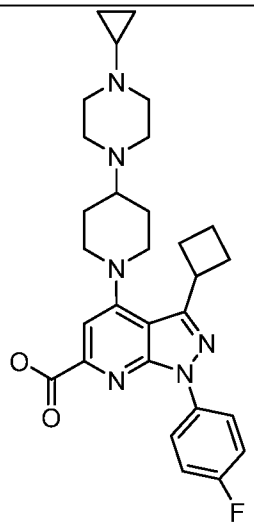
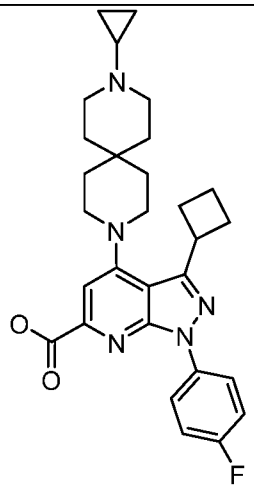
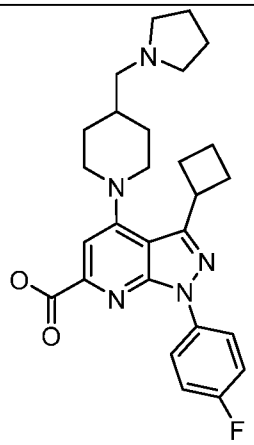
Int.	Structure	Name	SM	method	MW	Mes
A358		3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(3-methoxypyrrolidin-1-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E429	J1	493	494
A360		3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[1-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E460	J1	507	508
A361		3-cyclobutyl-1-(4-fluorophenyl)-4-{[4-(morpholin-4-yl)piperidin-1-yl]methyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP19	J13 Specific example	493	494

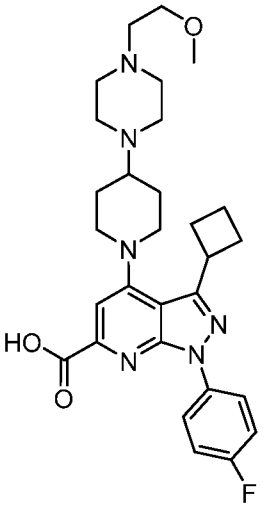
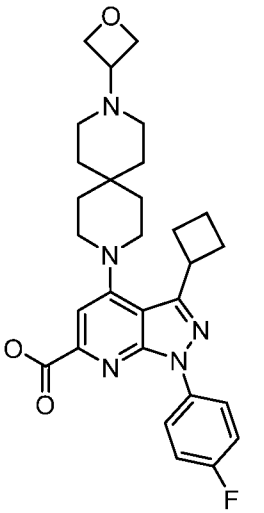
Int.	Structure	Name	SM	method	MW	Mes
A362		3-cyclobutyl-1-(4-fluorophenyl)-4-(4-hydroxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E492	J1	493	494
A363		4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E493	J1	493	494
A364		3-cyclobutyl-1-cyclohexyl-4-{4-[(morpholin-4-yl)methyl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP25, 364794-79-6	J14	474	475

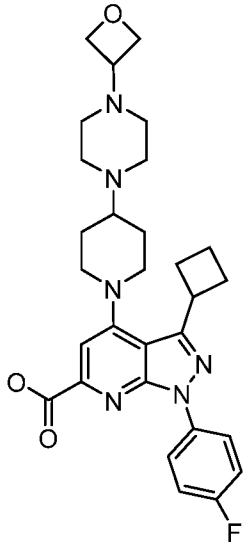
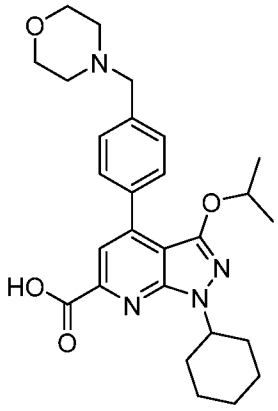
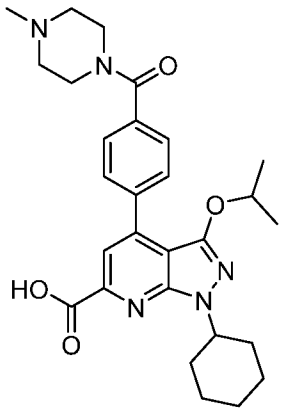
Int.	Structure	Name	SM	method	MW	Mes
A365		3-cyclobutyl-1-cyclohexyl-4-{4-[2-(morpholin-4-yl)ethyl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP25, 1150114-55-8	J14	488	489
A366		3-cyclobutyl-1-cyclohexyl-4-[4-(2-methylpyridin-4-yl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E461	J1	474	475
A367		3-cyclobutyl-1-cyclohexyl-4-{4-[1-(morpholin-4-yl)ethyl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP25, 1206594-12-8	J14	488	489

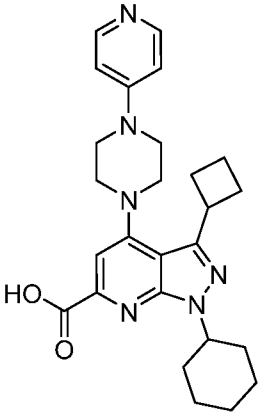
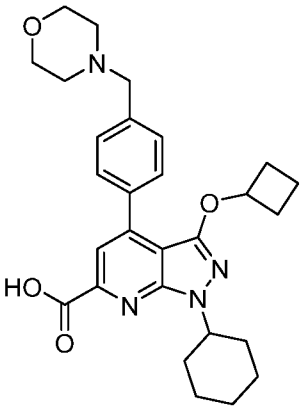
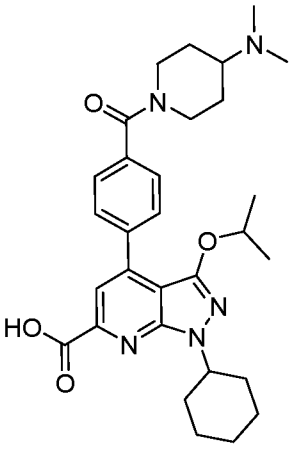
Int.	Structure	Name	SM	method	MW	Mes
A368		3-cyclobutyl-1-cyclohexyl-4-{4-[4-(propan-2-yl)piperazin-1-yl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP25, 1073354-18-3	J14	501	502
A369		3-cyclobutyl-1-cyclohexyl-4-[6-(4-methylpiperazin-1-yl)pyridin-3-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	A407, 109-01-3	J12	474	475
A370		3-cyclobutyl-1-cyclohexyl-4-{6-[4-(2-methoxyethyl)piperazin-1-yl]pyridin-3-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	A407, 13484-40-7	J12	518	519

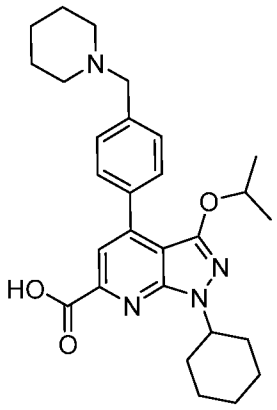
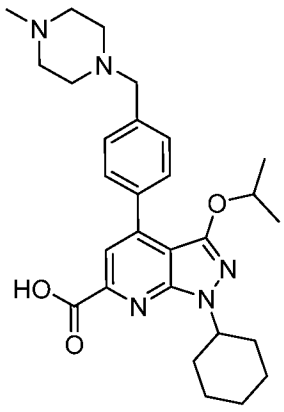
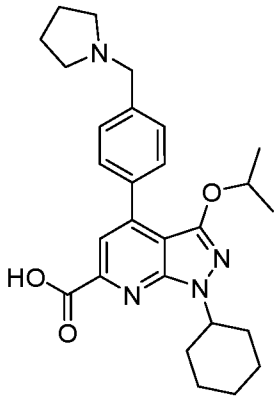
Int.	Structure	Name	SM	method	MW	Mes
A371		3-cyclobutyl-1-cyclohexyl-4-{4-[4-(propan-2-yl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E462	J1	508	509
A372		4-[(3*S*)-4-benzyl-3-methylpiperazin-1-yl]-3-cyclobutyl-1-cyclohexyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E463	J1	487	488
A373		4-[(3*R*)-4-benzyl-3-methylpiperazin-1-yl]-3-cyclobutyl-1-cyclohexyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E464	J1	487	488

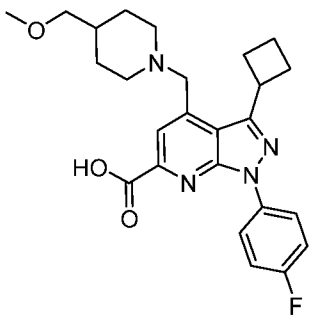
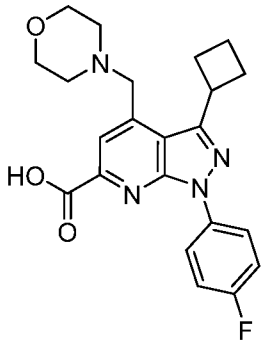
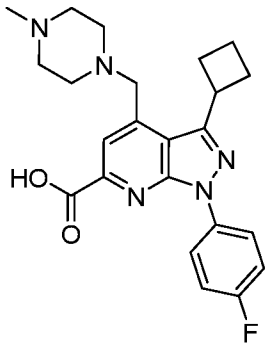
Int.	Structure	Name	SM	method	MW	Mes
A374		3-cyclobutyl-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E465	J1	518	519
A375		3-cyclobutyl-4-(9-cyclopropyl-3,9-diazaspiro[5.5]undecan-3-yl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E466	J1	503	504
A376		3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E467	J1	477	478

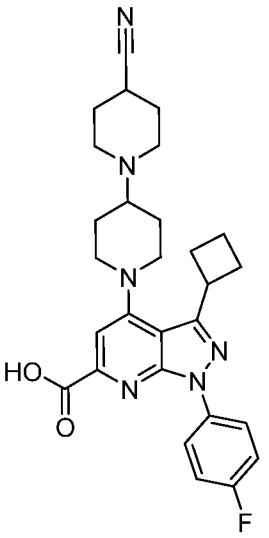
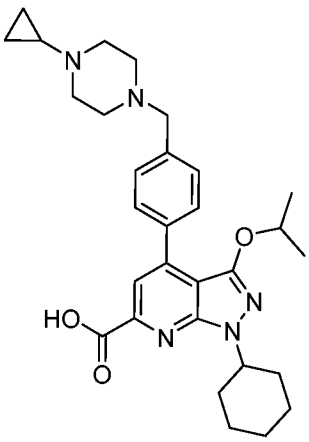
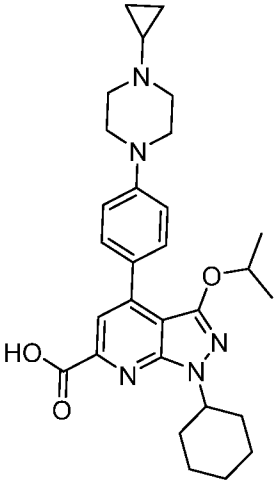
Int.	Structure	Name	SM	method	MW	Mes
A377		3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[4-(2-methoxyethyl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E468	J1	536	537
A378		3-cyclobutyl-1-(4-fluorophenyl)-4-[9-(oxetan-3-yl)-3,9-diazaspiro[5.5]undecan-3-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E469	J1	519	520

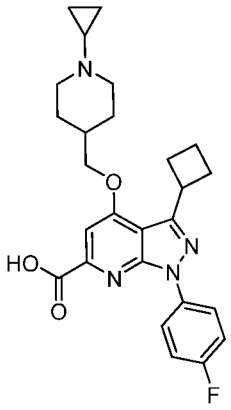
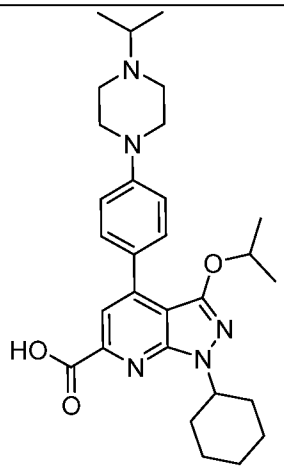
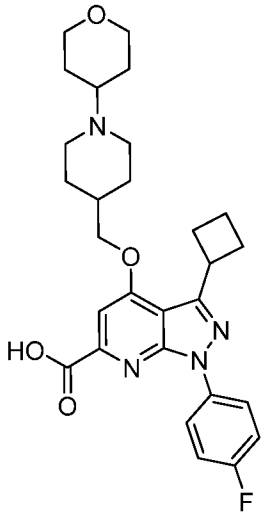
Int.	Structure	Name	SM	method	MW	Mes
A379		3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[4-(oxetan-3-yl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E470	J1	534	535
A380		1-cyclohexyl-4-{4-[(morpholin-4-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E473	J1	479	479
A381		1-cyclohexyl-4-[4-(4-methylpiperazine-1-carbonyl)phenyl]-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E474	J1	506	506

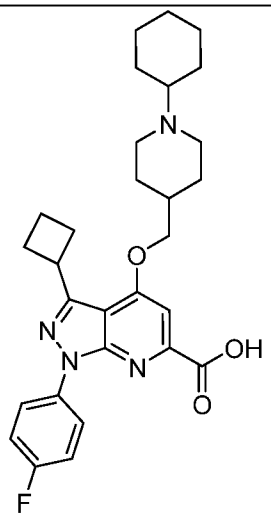
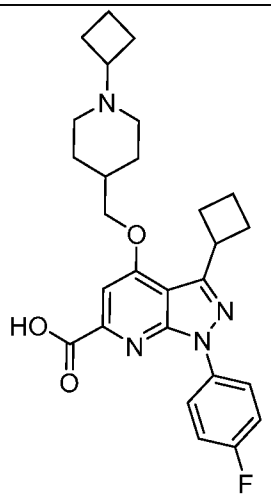
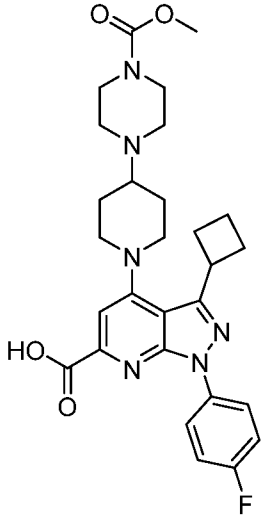
Int.	Structure	Name	SM	method	MW	Mes
A382		3-cyclobutyl-1-cyclohexyl-4-[4-(pyridin-4-yl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E475	J1	461	461
A383		3-(cyclobutyloxy)-1-cyclohexyl-4-{4-[(morpholin-4-yl)methyl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E476	J1	491	491
A384		1-cyclohexyl-4-{4-[4-(dimethylamino)piperidine-1-carbonyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E477	J1	534	535

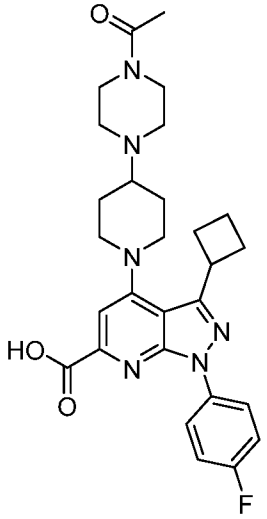
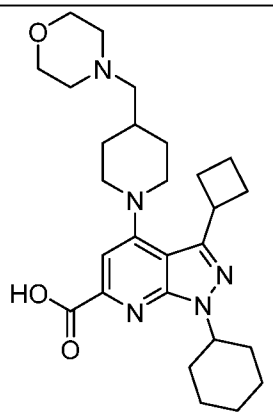
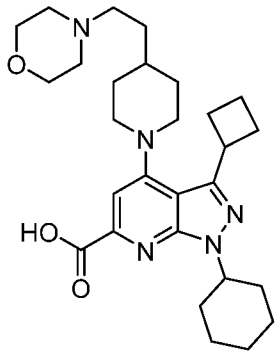
Int.	Structure	Name	SM	method	MW	Mes
A385		1-cyclohexyl-4-{4-[(piperidin-1-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E478	J1	477	477
A386		1-cyclohexyl-4-{4-[(4-methylpiperazin-1-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E479	J1	492	492
A387		1-cyclohexyl-3-[(propan-2-yl)oxy]-4-{4-[(pyrrolidin-1-yl)methyl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E480	J1	463	463

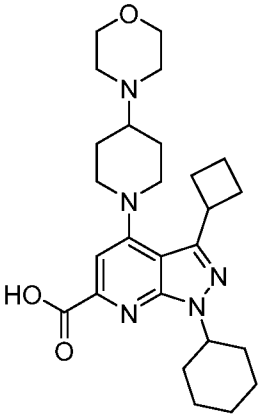
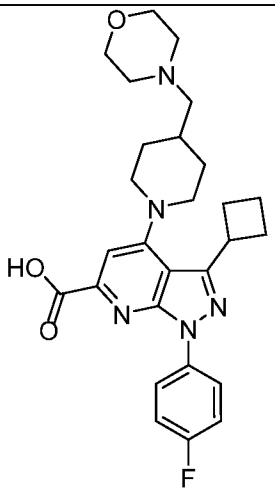
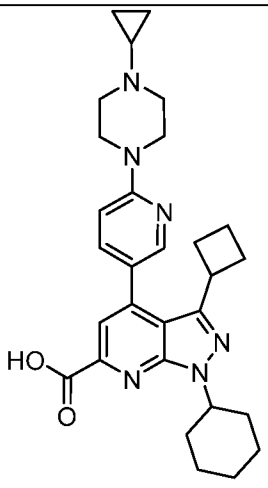
Int.	Structure	Name	SM	method	MW	Mes
A388		3-cyclobutyl-1-(4-fluorophenyl)-4-{[4-(methoxymethyl) piperidin-1-yl]methyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E481	J1	453	453
A389		3-cyclobutyl-1-(4-fluorophenyl)-4-[(morpholin-4-yl)methyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E471	J1	410	411
A390		3-cyclobutyl-1-(4-fluorophenyl)-4-[(4-methylpiperazin-1-yl)methyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E472	J1	423	424

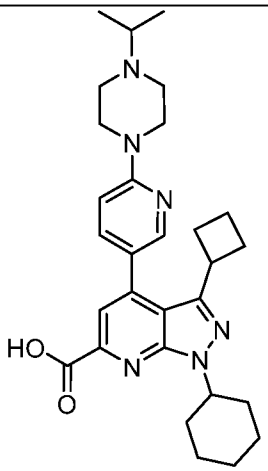
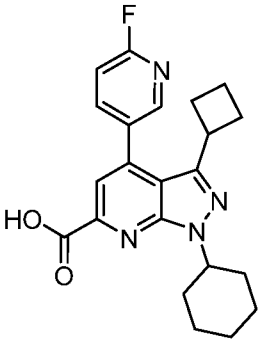
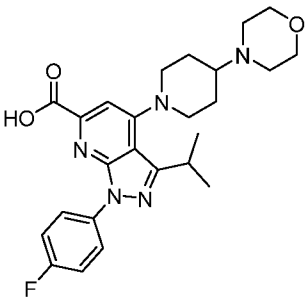
Int.	Structure	Name	SM	method	MW	Mes
A391		4-(4-cyano[1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E485	J1	502	503
A392		1-cyclohexyl-4-{4-[(4-cyclopropylpiperazin-1-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E482	J1	518	518
A393		1-cyclohexyl-4-[4-(4-cyclopropylpiperazin-1-yl)phenyl]-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E484	J1	503	504

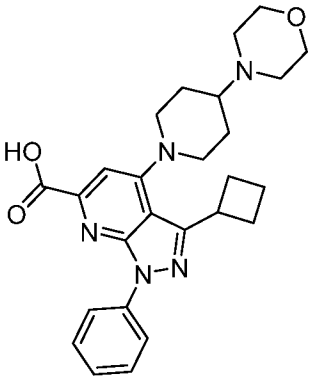
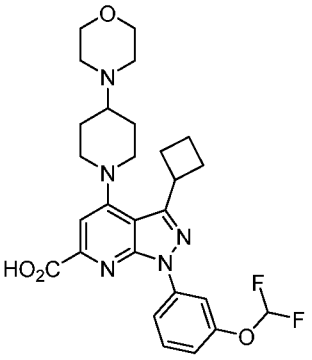
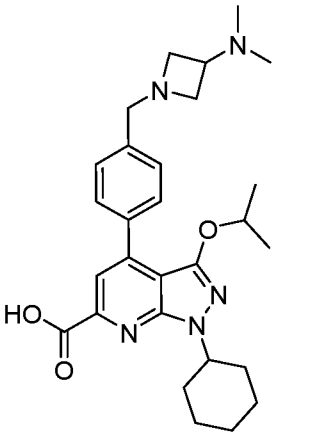
Int.	Structure	Name	SM	method	MW	Mes
A394		3-cyclobutyl-4-[(1-cyclopropylpiperidin-4-yl)methoxy]-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP26 ALC09	J3	464	465
A395		1-cyclohexyl-3-[(propan-2-yl)oxy]-4-{4-[4-(propan-2-yl)piperazin-1-yl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E483	J1	505	506
A396		3-cyclobutyl-1-(4-fluorophenyl)-4-{[1-(oxan-4-yl)piperidin-4-yl]methoxy}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP26 ALC08	J3	508	509

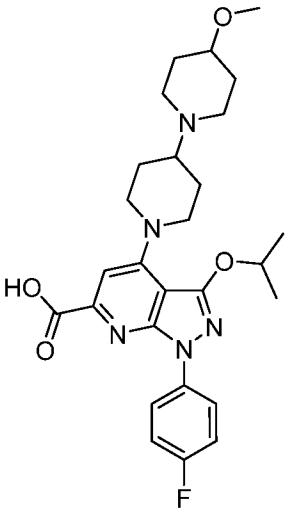
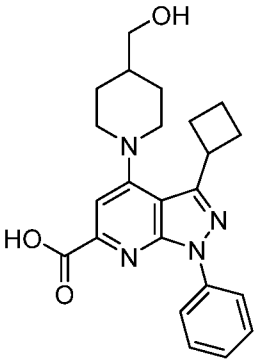
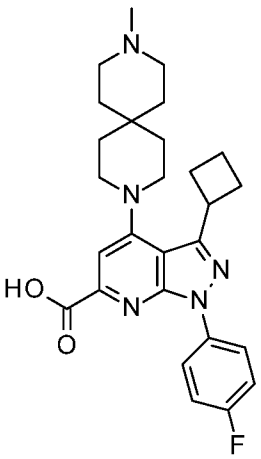
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A397		3-cyclobutyl-4-[(1-cyclohexylpiperidin-4-yl)methoxy]-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP26 ALC07	J3	506	507
A398		3-cyclobutyl-4-[(1-cyclobutylpiperidin-4-yl)methoxy]-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP26 ALC06	J3	478	479
A399		3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[4-(methoxycarbonyl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E486	J1	536	537

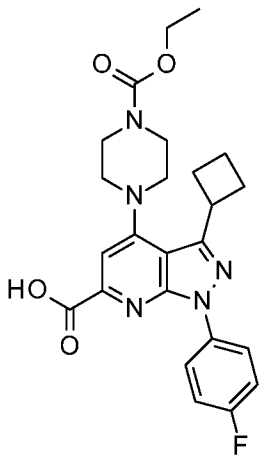
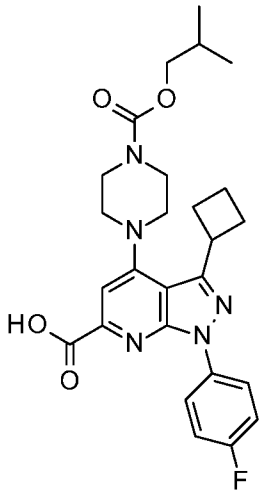
Int.	Structure	Name	SM	method	MW	Mes
A400		4-[4-(4-acetylpiperazin-1-yl)piperidin-1-yl]-3-cyclobutyl-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E487	J1	520	521
A401		3-cyclobutyl-1-cyclohexyl-4-{4-[(morpholin-4-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E488	J1	481	482
A402		3-cyclobutyl-1-cyclohexyl-4-{4-[2-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E489	J1	495	496

Int.	Structure	Name	SM	method	MW	Mes
A403		3-cyclobutyl-1-cyclohexyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E490	J1	467	468
A404		3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[(morpholin-4-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E491	J1	493	494
A405		3-cyclobutyl-1-cyclohexyl-4-[6-(4-cyclopropylpiperazin-1-yl)pyridin-3-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	A407, 20327-23-5	J12 Specific example	500	501

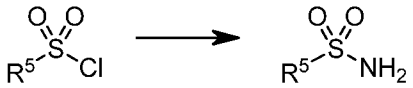
Int.	Structure	Name	SM	method	MW	Mes
A406		3-cyclobutyl-1-cyclohexyl-4-{6-[4-(propan-2-yl)piperazin-1-yl]pyridin-3-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	A407, 4318-42-7	J12	502	503
A407		3-cyclobutyl-1-cyclohexyl-4-(6-fluoropyridin-3-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP25, 351019-18-6	J14	394	395
A408		1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP11, 442563-55-5	J10 Specific example	467	468

Int.	Structure	Name	SM	method	MW	Mes
A409		3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10	J10	461	462
A410		3-cyclobutyl-1-[3-(difluoromethoxy)phenyl]-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E510	J1	527	528
A411		1-cyclohexyl-4-(4-{[3-(dimethylamino)azetidin-1-yl]methyl}phenyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E426	J1A	491	492

Int.	Structure	Name	SM	method	MW	Mes
A412		1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E511	J1A	511	512
A413		3-cyclobutyl-4-[4-(hydroxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	HP10	J10, Specific example	406	407
A414		3-cyclobutyl-1-(4-fluorophenyl)-4-(9-methyl-3,9-diazaspiro[5.5]undecan-3-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E515	J1	477	478

Int.	Structure	Name	SM	method	MW	Mes
A415		3-cyclobutyl-4-[4-(ethoxycarbonyl) piperazin-1-yl]-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E516	J1	467	468
A416		3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[(2-methylpropoxy)carbonyl]piperazin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E517	J1	495	496

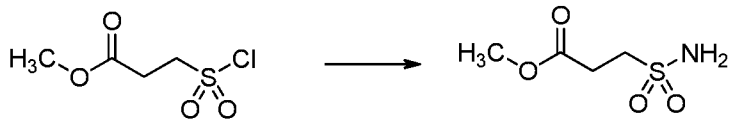
Method X1: Synthesis of sulfonamide



[00700] A procedure similar to that described in J. Org. Chem. (1968) 33(2), 897 is followed: A round bottomed flask is charged with the sulfonyl chloride and diethyl ether (0.06 M), sealed with a septum and cooled in an ice bath. To the cooled solution is slowly added two molar equivalents of a dioxane solution of ammonia (0.5 M), and then the cold bath is removed. After 16 hours, the resulting heterogeneous mixture is filtered through filter paper. Volatiles are

removed from the filtrate via rotary evaporation to give the sulfonamide which is used without further purification.

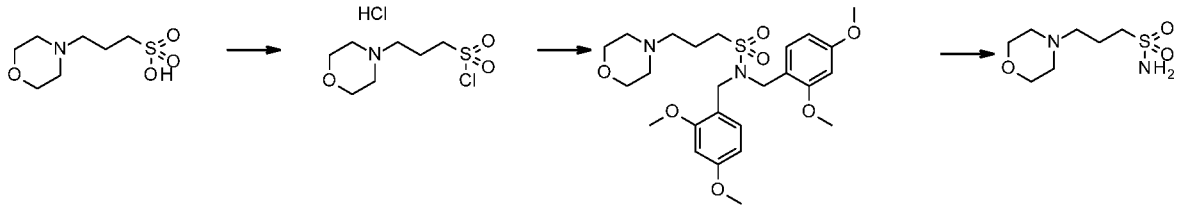
Illustrative synthesis of S2: methyl 3-sulfamoylpropanoate



[00701] A dioxane solution of ammonia (0.5 M, 10.5 mL, 5.25 mmol, 2.05 equiv) was added at 0 °C to a solution of methyl 3-(chlorosulfonyl)propanoate (CAS: 15441-07-3, 0.476 g, 2.55 mmol) in diethyl ether (10 mL). The reaction mixture was stirred at 0 °C for 1 hour and then 16 hours at RT. The reaction mixture was filtered, and the filtrate was concentrated to give the titled compound which was used without further purification.

Method X2: Synthesis of sulfonamide

Synthesis of 3-morpholinopropane-1-sulfonamide S10



[00702] *Step 1: 3-(morpholin-4-yl)propane-1-sulfonyl chloride*

[00703] 3-Morpholinopropanesulfonic acid (CAS: 1132-61-2, 0.63 g, 3.0 mmol) was added to thionyl chloride (4.0 mL, 54.8 mmol, 18 equiv). Dimethylformamide (0.1 mL, 1.2 mmol, 0.4 equiv) was added, and the reaction mixture was stirred at RT for 5 hours. The reaction mixture was diluted with dichloromethane (4 mL) and dropped into heptane. Precipitation occurred, and the supernatant was removed. The residue dissolved in dichloromethane was dropped into pentane. The supernatant was removed, and the solid dried to give 3-morpholinopropanesulfonyl chloride hydrochloride.

[00704] *Step 2: N,N-bis[(2,4-dimethoxyphenyl)methyl]-3-(morpholin-4-yl)propane-1-sulfonamide*

[00705] Bis(2,4-dimethoxybenzyl)amine (CAS: 20781-23-1, 0.32 g, 1.0 mmol, 1.0 equiv) and potassium carbonate (0.28 g, 2.0 mmol, 2.0 equiv) were added to a solution of 3-

morpholinopropanesulfonyl chloride hydrochloride (0.26 g, 1.0 mmol) in acetonitrile (20 mL). The reaction mixture was stirred at RT for 8 hours. The reaction mixture was concentrated and the residue partitioned between water and ethyl acetate. The organic phase was dried over sodium sulfate, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography eluting with heptane/ethyl acetate (100/0 to 0/100) to give *N,N*-bis[(2,4-dimethoxyphenyl)methyl]-3-morpholino-propane-1-sulfonamide.

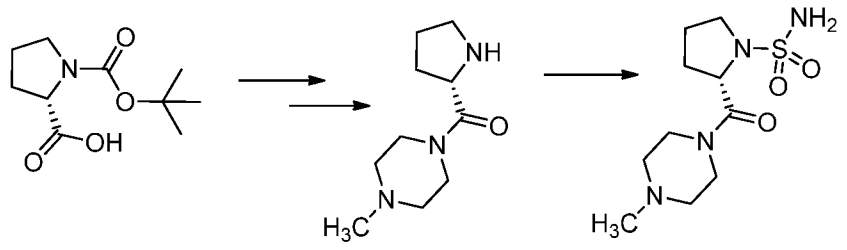
[00706] *Step 3: 3-(morpholin-4-yl)propane-1-sulfonamide*

[00707] Trifluoroacetic acid (0.8 mL, 10.4 mmol, 39 equiv) was added to a solution of *N,N*-bis[(2,4-dimethoxyphenyl)methyl]-3-morpholino-propane-1-sulfonamide (0.135 g, 0.27 mmol) in dichloromethane (4 mL). The reaction mixture was stirred at RT for 16 hours and was added to a saturated aqueous solution of sodium hydrogencarbonate. The mixture was extracted with ethyl acetate and then with a 9:1 mixture of dichloromethane/isopropanol. The organic phases were dried over sodium sulfate, filtered and concentrated under reduced pressure to give the titled compound.

[00708] As an alternative preparation of S10, 3-chloropropane-1-sulfonamide (3.15 g, 20.0 mmol), morpholine (1.84, 21.0 mmol), sodium carbonate (4.24 g, 40.0 mmol) and sodium iodide (300 mg, 2.0 mmol) were heated in anhydrous dioxane (70 mL) at 70 °C for a day. The suspension was permitted to cool towards room temperature and then filtered through diatomaceous earth with an MTBE rinse. The filtrate was concentrated and chromatographed on silica (0 to 4% concentrated aqueous NH_4OH/CH_3CN) to give the titled compound (1.47 g). ^1H NMR (400 MHz, $CDCl_3$) δ ppm 5.41 (s, 2H), 3.70 (t, J = 4.7 Hz, 4H), 3.23 (t, J = 7.2 Hz, 2H), 2.54-2.43 (m, 6H), 2.10-2.02 (m, 2H); MS (DCI) *m/z* 209 $(M+H)^+$.

Method X3. Synthesis of sulfonamide

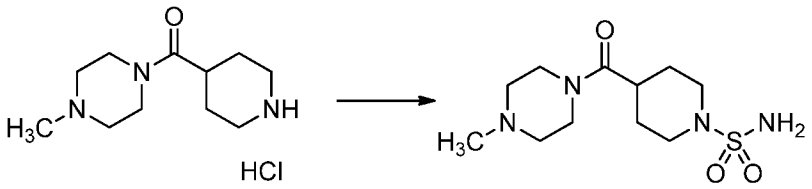
Synthesis of (2S)-2-(4-methylpiperazine-1-carbonyl)pyrrolidine-1-sulfonamide S11



[00709] The titled compound may be prepared by the method described in Ebden, et al. PCT Int. Appl. WO2004 011443, example 25, substituting *N*-methylpiperidine hydrochloride for dimethylamine hydrochloride. To 1-(*tert*-butoxycarbonyl)-L-proline (5.0 g) in DCM (50 mL) at 5 °C was added dicyclohexylcarbodiimide (5.22 g) and *N*-hydroxysuccinimide (2.91 g). The mixture was stirred at this temperature for 16 hours. The solid was filtered, and the filtrate cooled to 5 °C. To this mixture was added triethylamine (9.80 mL) and *N*-methylpiperidine hydrochloride (4.7 g). The mixture was stirred at room temperature for 2 days, H_2O (50 mL) was added, and the phases were separated. The organic fraction was washed with saturated sodium carbonate (2×20 mL) and brine (20 mL). This was then dried ($MgSO_4$) and concentrated to dryness to afford *tert*-butyl (2*S*)-2-(4-methylpiperazine-1-carbonyl)pyrrolidine-1-carboxylate. This was then treated with 4 M aqueous HCl (20 mL), stirred at room temperature 3 hours, and concentrated in vacuo to dryness. A solution of the residue in dioxane was then treated with 2 grams of triethylamine and 10 grams of sulfamide, and the mixture was heated at reflux for 3 days before cooling. Solids were removed by filtration and washed with methanol. The combined filtrate and washing are concentrated in vacuo, and the residue was purified by column chromatography to give the titled compound.

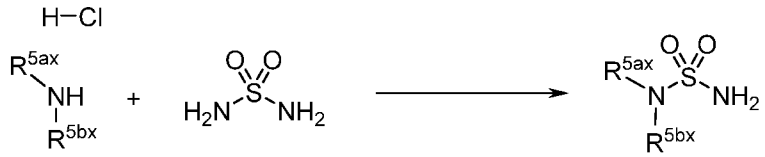
Method X4. Synthesis of sulfonamide

Synthesis of 4-(4-methylpiperazine-1-carbonyl)piperidine-1-sulfonamide S12



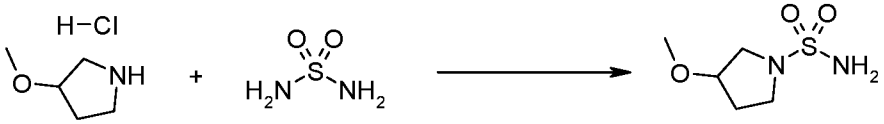
[00710] A solution of (4-methylpiperazin-1-yl)(piperidin-4-yl)methanone hydrochloride in dioxane was treated with 5 equivalents of triethylamine and 10 equivalents of sulfamide and heated at reflux for 3 days. The mixture was then cooled and filtered, and the solids were washed with methanol. The filtrate and washings were concentration in vacuo, and the residue was purified by column chromatography to give the titled compound.

Method X4B. Synthesis of sulfamides



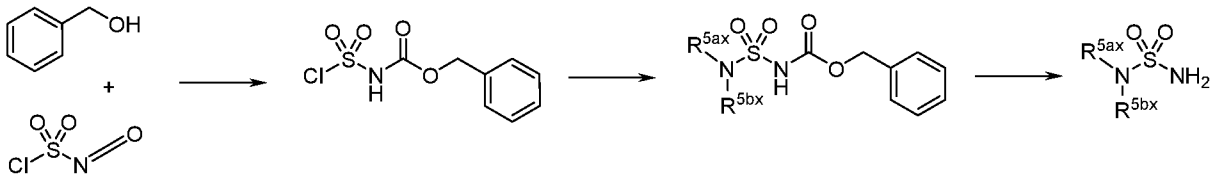
[00711] A solution of amine hydrochloride (from 1 to 2 equiv.) in dioxane is treated with triethylamine (from 1.1 to 2.2 equiv), and sulfamide (from 1 to 2 equiv) and refluxed until full conversion is observed. The mixture is then cooled to RT, and the residue is purified by flash column chromatography to give the desired sulfamide derivative.

Illustrative synthesis of compound S14



[00712] A solution of 3-methoxypyrrolidine hydrochloride ([136725-50-3], 136 mg, 0.98 mmol) in dioxane (2 mL) was treated with triethylamine (0.2 mL, 1.4 mmol) and sulfamide (7803-58-9, 130 mg, 1.3 mmol), and the mixture was refluxed for 16 hours. The mixture was then cooled to RT, and the residue was purified by column chromatography eluted with DCM/MeOH (9/1) to give the titled compound.

Method X5. Synthesis of sulfamides



[00713] *Step 1: benzyl (chlorosulfonyl)carbamate*

[00714] A solution of chlorosulfonylisocyanate ([1189-71-5], 1 eq) in anhydrous DCM (2.5 vol.) is cooled down in an ice batch under argon atmosphere. Benzyl alcohol ([100-51-6], 1 eq) is added dropwise over a 15 minutes period. The reaction mixture is stirred for 5 minutes and allowed to warm up to RT. The reaction mixture is worked up when no more starting material remained, by adding *n*-pentane. The precipitate is filtered, washed with *n*-pentane, and dried at 40 °C under reduced pressure to give the titled compound.

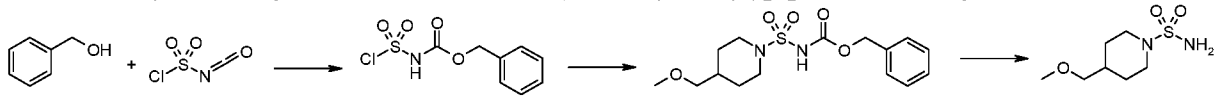
[00715] *Step 2: N-Benzyloxycarbonyl protected sulfamide*

[00716] A solution of amine (1 eq) and *N*,*N*-diisopropylethylamine (1.2 eq) in anhydrous DCM (10 vol.) is cooled down in an ice bath under an argon atmosphere. The compound from Step 1 (1.2 eq) is added, and after 5 minutes, the solution is allowed to warm up to RT. The reaction mixture is worked up when no more starting material remained, by adding water. The organic phase is diluted, separated, and washed successively with an aqueous 1 M HCl solution and a saturated aqueous solution of NaCl. The organic phase is dried over magnesium sulfate, filtered and concentrated in vacuo. The crude sample is either purified by flash column chromatography or suspended in a mixture of *n*-heptane/ethyl acetate (9/1), refluxed for 15 minutes, and then left cooling down to RT. The precipitate is collected by filtration, washed with a mixture of *n*-heptane/ethyl acetate (9/1), and dried at 40 °C under reduced pressure to give the desired *N*-benzyloxycarbonyl protected sulfamide.

[00717] *Step* 3: *N-Deprotected sulfamide*

[00718] A solution of *N*-benzyloxycarbonyl protected sulfamide (1 eq) in THF or MeOH (20 vol.) is degassed with nitrogen. 20% $Pd(OH)_2$ w/w is added, and the reaction mixture is purged with H_2. The mixture is stirred at room temperature under a hydrogen atmosphere (balloon) until no more starting material is observed. Additional 20% $Pd(OH)_2$ is added if necessary. The reaction mixture is filtered over a diatomaceous earth pad that is washed with THF or MeOH. The filtrate is concentrated in vacuo. The residue is purified by preparative HPLC or by flash column chromatography or used as such in the next step.

Illustrative synthesis of intermediate S15: 4-(methoxymethyl)piperidine-1-sulfonamide



[00719] *Step 1: benzyl (chlorosulfonyl)carbamate*

[00720] A solution of chlorosulfonylisocyanate ([1189-71-5], 8.1 g, 57.4 mmol) in anhydrous DCM (20 mL) was cooled down in an ice bath under an argon atmosphere. Benzyl alcohol ([100-51-6], 5.9 mL, 57.4 mmol) was added dropwise over a 15 minutes period. The reaction mixture was stirred for 5 minutes and allowed to warm up to RT. After 10 minutes, *n*-pentane (20 mL) was added, and the resulting mixture was stirred at RT for 30 minutes. The precipitate was collected by filtration, washed with *n*-pentane, and dried at 40 °C under reduced pressure to give the titled compound.

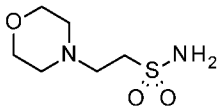
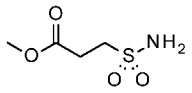
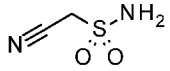
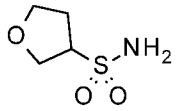
[00721] *Step 2: benzyl [4-(methoxymethyl)piperidine-1-sulfonyl]carbamate*

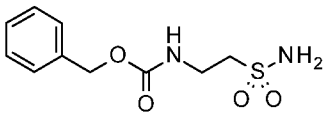
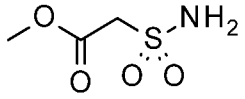
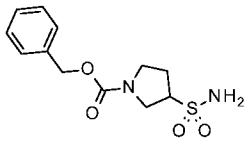
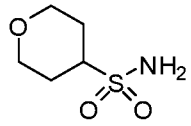
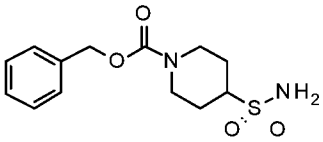
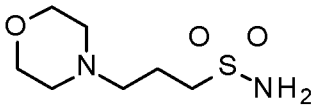
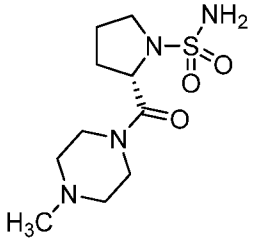
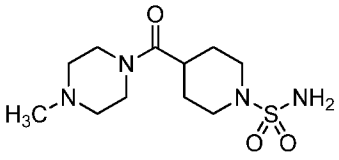
[00722] A solution of 4-(methoxymethyl)piperidine hydrochloride ([399580-55-3], 1.0 g, 6.0 mmol) and *N*,*N*-diisopropylethylamine (2.3 mL, 13.3 mmol) in anhydrous DCM (10 mL) was cooled down in an ice bath under an argon atmosphere. Benzyl (chlorosulfonyl)carbamate from Step 1 (1.8 g, 7.2 mmol) was added and after 5 minutes, and the solution was allowed to warm up to RT. After 3 hours, water (10 mL) and DCM (10 mL) were added, and stirring was continued for 15 minutes. The organic phase was separated, washed successively with an aqueous 1 M HCl solution (2 x 10 mL), and a saturated aqueous solution of NaCl (10 mL). The organic phase was dried over magnesium sulfate, filtered and concentrated in vacuo. The residue was purified by flash column chromatography eluting with a gradient of DCM/MeOH to give the titled compound.

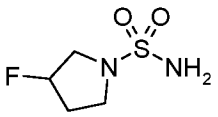
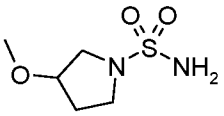
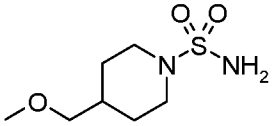
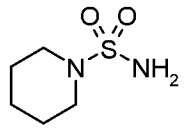
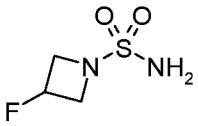
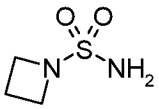
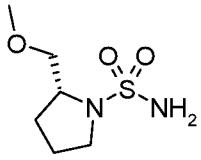
[00723] *Step 3: 4-(methoxymethyl)piperidine-1-sulfonamide*

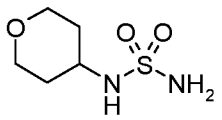
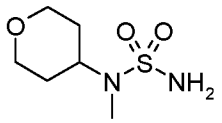
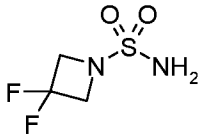
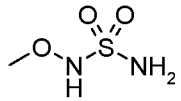
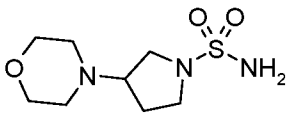
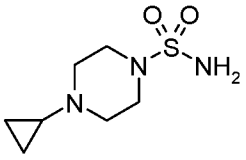
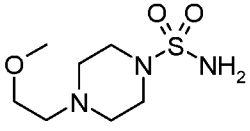
[00724] A solution of compound from Step 2 (570 mg, 1.8 mmol) in THF (11 mL) was degassed with nitrogen. 20% $Pd(OH)_2$ (w/w, 114 mg) was added, and the reaction mixture was purged with H_2. The mixture was stirred for 20 hours at RT under a hydrogen atmosphere (balloon). The reaction mixture was filtered over a diatomaceous earth pad that was washed with THF. The filtrate was concentrated in vacuo to give the titled compound.

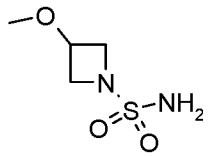
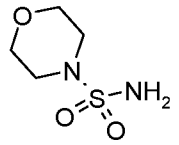
Table XIV. List of sulfonamides

Int.	Structure	Name	SM	method	MW	Mes
S1		2-morpholinoethanesulfonamide	103654-84-8	X1	194	
S2		methyl 3-sulfamoylpropanoate	15441-07-3	X1 Specific example	167	
S3		cyanomethanesulfonamide	27869-04-1	X1	120	
S4		tetrahydrofuran-3-sulfonamide	1207346-29-9	X1	151	

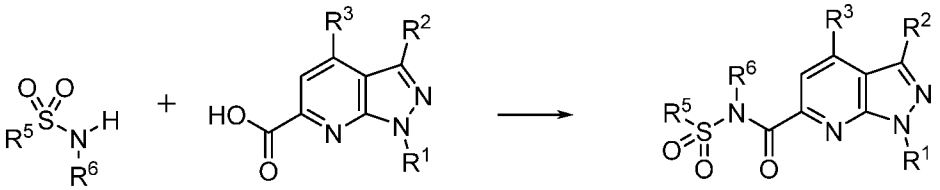
Int.	Structure	Name	SM	method	MW	Mes
S5		benzyl *N*-(2-sulfamoylethyl)carbamate	52530-50-4	X1	258	259
S6		methyl 2-sulfamoylacetate	52530-50-4	X1	153	
S7		benzyl 3-sulfamoylpyrrolidine-1-carboxylate	1035173-74-0	X1	284	
S8		tetrahydro-2*H*-pyran-4-sulfonamide	1058131-55-7	X1	165	
S9		benzyl 4-sulfamoylpiperidine-1-carboxylate	287953-54-2	X1	298	
S10		3-morpholinopropane-1-sulfonamide	1132-61-2	X2 Specific example	208	209
S11		(2*S*)-2-(4-methylpiperazine-1-carbonyl)pyrrolidine-1-sulfonamide	15761-39-4	X3 Specific example	276	
S12		4-(4-methylpiperazine-1-carbonyl)piperidine-1-sulfonamide	1018826-44-2	X4 Specific example	290	

Int.	Structure	Name	SM	method	MW	Mes
S13		3-fluoropyrrolidine-1-sulfonamide	7803-58-9, 169750-17-8	X4B	168	
S14		3-methoxypyrrolidine-1-sulfonamide	7803-58-9, 136725-50-3	X4B Specific example	180	
S15		4-(methoxymethyl)piperidine-1-sulfonamide	1189-71-5, 399580-55-3	X5 Specific example	208	
S16		piperidine-1-sulfonamide	1189-71-5, 110-89-4	X5	164	
S17		3-fluoroazetidine-1-sulfonamide	1189-71-5, 617718-46-4	X5	154	
S18		azetidine-1-sulfonamide	1189-71-5, 503-29-7	X5	136	
S19		(2*R*)-2-(methoxymethyl)pyrrolidine-1-sulfonamide	1189-71-5, 84025-81-0	X5	194	

Int.	Structure	Name	SM	method	MW	Mes
S20		*N*-oxan-4-ylsulfuric diamide	1189-71-5, 38041-19-9	X5	180	
S21		*N*-methyl-*N*-oxan-4-ylsulfuric diamide	1189-71-5, 220641-87-2	X5	194	
S22		3,3-difluoroazetidine-1-sulfonamide	1189-71-5, 288315-03-7	X5	172	
S23		*N*-methoxysulfuric diamide	1189-71-5, 593-56-6	X5	126	
S24		3-(morpholin-4-yl)pyrrolidine-1-sulfonamide	1189-71-5, 53617-37-1	X5	235	
S25		4-cyclopropylpiperazine-1-sulfonamide	1189-71-5, 20327-23-5	X5	205	
S26		4-(2-methoxyethyl)piperazine-1-sulfonamide	1189-71-5, 13484-40-7	X5	223	

Int.	Structure	Name	SM	method	MW	Mes
S27		3-methoxyazetidine-1-sulfonamide	1189-71-5, 148644-09-1	X5	166	
S28		morpholine-4-sulfonamide	1189-71-5, 110-91-8	X5	166	

Method Y1: Synthesis of acylsulfonamide and acylsulfamate from carboxylic acid

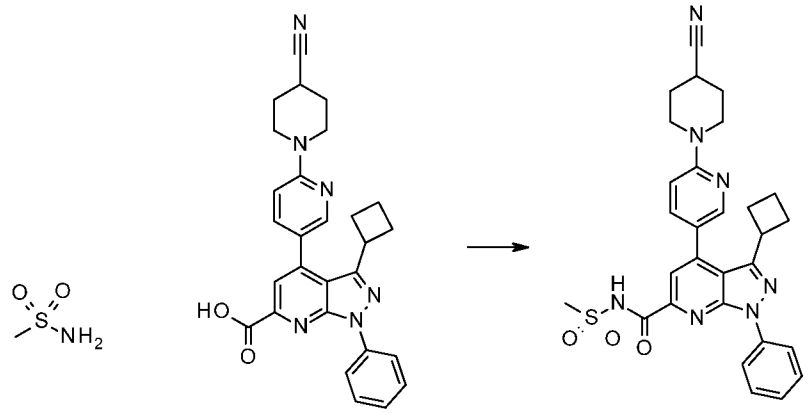


[00725] EDC•HCl (CAS 25952-538, 1.0 to 4.0 equiv) is added at RT to a stirring solution of carboxylic acid, sulfonamide or sulfamate (from 1.0 to 4.0 equiv) and 4-(dimethylamino) pyridine (CAS 1122-58-3, from 0.1 to 2.0 equiv) in dichloromethane or/and THF or/and acetone or/and acetonitrile. The reaction mixture is stirred at RT until full conversion is observed. The reaction mixture can be worked up or the solvent can be evaporated and the residue is purified by precipitation, by flash column chromatography or by preparative HPLC to yield the titled acylsulfonamide or acylsulfamide. To work up the reaction mixture, the solvent can be evaporated, and the residue is then partitioned between dichloromethane and water. The organic phase is successively washed with a saturated aqueous solution of $NaHCO_3$, aqueous 0.5 N HCl and brine. The organic phase is separated, dried over sodium sulfate, filtered and concentrated in vacuo. Alternatively, the reaction mixture may be concentrated without an extractive workup. The residue is purified either by precipitation, by flash column chromatography or by preparative HPLC to yield the titled acylsulfonamide or acylsulfamate.

[00726] Alternatively, acylsulfonamides or acylsulfamates can be prepared in the following manner. A solution of the carboxylic acid (1 eq) in dichloromethane, dichloroethane or dimethylformamide can be treated with carbodiimidazole (1-2.5 eq) stirred at ambient

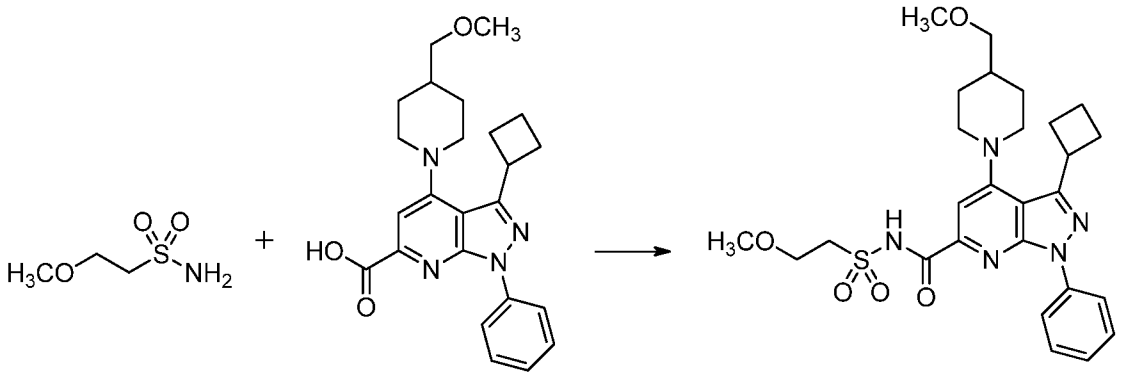
temperature to 65 °C for from 0.5-3 hours. Then the sulfonamide or sulfamate (1-3 eq) and optional potassium bis(trimethylsilyl)amide, sodium hydride, or triethylamine followed by 1,8-diazabicycloundec-7-ene (1-3 eq) and optional 4-(dimethylamino)pyridine (1-2 eq) can be added, and the reaction mixture is stirred at 20-60 °C for 2-16 hours. The reaction mixture can then be concentrated and the residue purified.

Illustrative synthesis of compound 71: 4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-cyclobutyl-N-(methanesulfonyl)-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



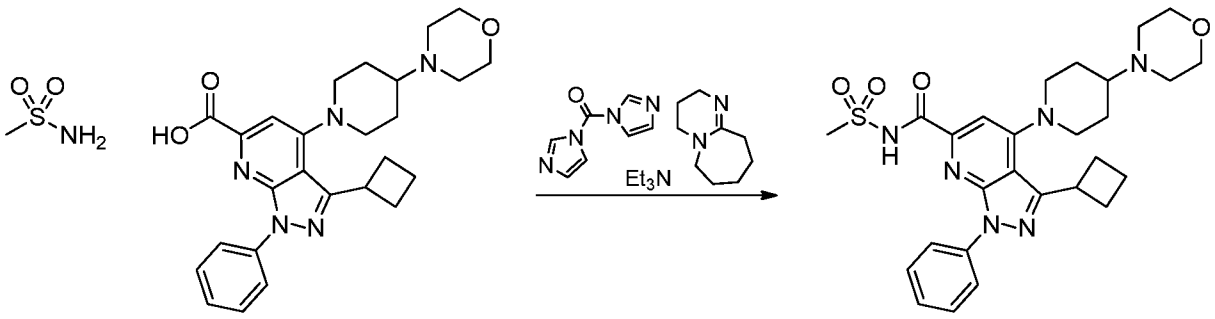
[00727] EDC•HCl (CAS 25952-538, 24.6 g, 128.3 mmol) was added at RT to a stirring solution of intermediate A056 (30.7g, 64.1 mmol), methanesulfonamide (CAS 3144-09-0, 12.2 g, 128.3 mmol) and 4-(dimethylamino) pyridine (CAS 1122-58-3, 3.1 g, 25.7 mmol) in DCM (1L). The reaction mixture was stirred at RT for 1.5 hours. The solution was diluted with DCM (700 mL), washed successively with a saturated aqueous solution of sodium hydrogencarbonate (500 mL), aqueous 0.5 N HCl (500 mL) and a saturated aqueous solution of NaCl (500 mL). The organic phase was dried over sodium sulfate, filtered and concentrated under reduced pressure. The crude sample was purified by flash column chromatography eluting with DCM/ethyl acetate. The compound was suspended in acetonitrile and refluxed until complete dissolution. The warm solution was poured in hot water (700 mL), and the mixture was refluxed for 2 hours. The reaction volume was reduced to one third under a flow of nitrogen at 80 °C. The precipitate was collected by filtration and dried at 40 °C under reduced pressure.

Illustrative synthesis of compound 256: 3-cyclobutyl-N-(2-methoxyethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



[00728] To a 4 mL vial charged with stir bar was added 3-cyclobutyl-4-[4-(methoxymethyl)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (A136, 40 mg, 0.095 mmol) dissolved in 600 µL of dichloroethane followed by carbodiimidazole (34 mg, 0.21 mmol) in 600 µL of dichloroethane. The mixture was stirred at 42 °C for two hours. Then 2-methoxyethanesulfonamide (40 mg, 3 eq, 0.28 mmol) was then added followed by 1,8-diazabicycloundec-7-ene (43 uL, 3 eq, 0.28 mmol). The resultant mixture was heated at 60 °C for 16 hours. After completion of reaction, the reaction mixture was concentrated, dissolved in DMSO, and purified by reverse phase HPLC (C18, 0-100% CH_3CN/water (0.1% TFA)). A gradient of acetonitrile (A) and 0.1% trifluoroacetic acid in water (B) was used, at a flow rate of 50 mL/min (0-0.5 min 10% A, 0.5-6.0 min linear gradient 10-100% A, 6.0-7.0 min 100% A, 7.0-8.0 min linear gradient 100-10% A) to afford the title compound.

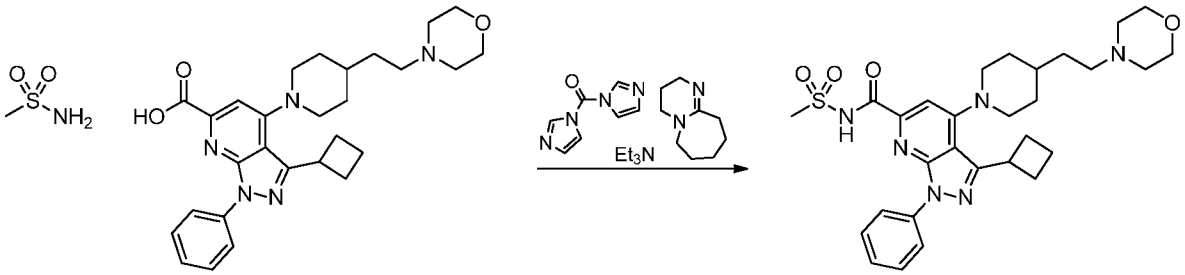
Illustrative synthesis of compound 328: 3-cyclobutyl-N-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



[00729] 3-Cyclobutyl-4-(4-morpholino-1-piperidyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (A268, 139 mg, 0.30 mmol) and carbonyl diimidazole (73 mg, 0.45 mmol) were stirred in anhydrous DMF (2 mL) at room temperature for 50 minutes. Then

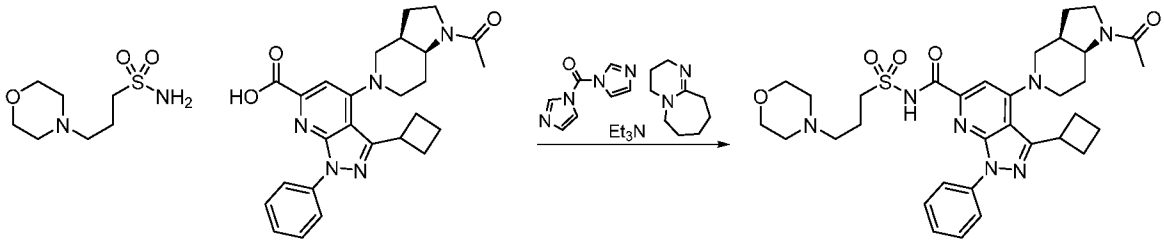
methanesulfonamide (57 mg, 0.60 mmol) was added, followed by triethylamine (125 µL, 0.90 mmol), and the suspension was stirred overnight. DBU (45 µL, 0.30 mmol) was added dropwise to the suspension, which was stirred for more than forty minutes before additional DBU (22.5 µL, 0.15 mmol) was added, and the solution was heated at 50 °C for more than 4 hours. The reaction mixture was then purified by preparative HPLC on a preparatory Waters® Atlantis® T3 column (30 mm × 100 mm) with a 20 to 100% gradient of acetonitrile in 10 mM aqueous ammonium acetate at 40 mL/min to give the titled compound (70 mg).

Illustrative synthesis of compound 331: 3-cyclobutyl-N-(methanesulfonyl)-4-{4-[2-(morpholin-4-yl)ethyl]piperidin-1-yl}-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



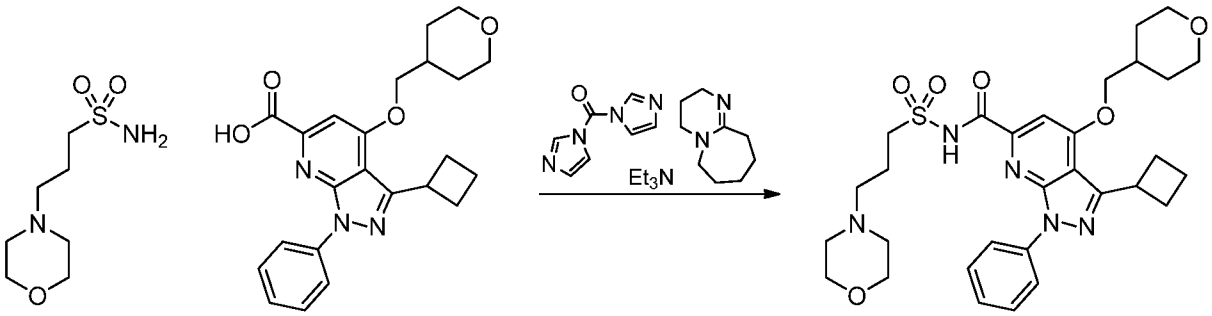
[00730] 3-Cyclobutyl-4-[4-(2-morpholinoethyl)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (A270, 118 mg, 0.24 mmol) and carbonyl diimidazole (78 mg, 0.48 mmol) were stirred in anhydrous DMF (1.5 mL) at room temperature for one hour. Then methanesulfonamide (46 mg, 0.48 mmol) and triethylamine (67 µL, 0.48 mmol) were added, followed by slow, dropwise addition of DBU (54 µL, 0.36 mmol). The reaction mixture was stirred for about another 30 minutes, diluted with water (8 mL), concentrated and purified by preparative HPLC on a preparatory Waters® Atlantis® T3 column (30 mm × 100 mm) with a 20 to 100% gradient of acetonitrile in 10 mM aqueous ammonium acetate at 40 mL/min to give the titled compound (46 mg).

Illustrative synthesis of compound 332: 4-[(3aR,7aS)-1-acetyloctahydro-5H-pyrrolo[3,2-c]pyridin-5-yl]-3-cyclobutyl-N-[3-(morpholin-4-yl)propane-1-sulfonyl]-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



[00731] 4-[(3a*R*,7a*S*)-1-Acetyl-3,3a,4,6,7,7a-hexahydro-2*H*-pyrrolo[3,2-*c*]pyridin-5-yl]-3-cyclobutyl-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (A271, <0.5 mmol) and carbonyl diimidazole (243 mg, 1.5 mmol) were stirred in anhydrous DMF (4 mL) at room temperature for an hour. Then triethylamine (210 μL, 1.5 mmol) and a solution of 3-(morpholin-4-yl)propane-1-sulfonamide (S10, 313 mg, 1.5 mmol) in anhydrous acetonitrile (400 μL) were added, followed by slow dropwise addition of DBU (75 μL, 0.50 mmol). The reaction mixture was stirred for an hour, more DBU (45 μL, 0.30 mmol) was added dropwise, and the reaction mixture was stirred another hour before being diluted with water (20 mL), concentrated and purified by preparative HPLC on a preparatory Waters® Atlantis® T3 column (30 mm × 100 mm) with a 5 to 100% gradient of acetonitrile in 10 mM aqueous ammonium acetate at 40 mL/min to give the titled compound (74 mg).

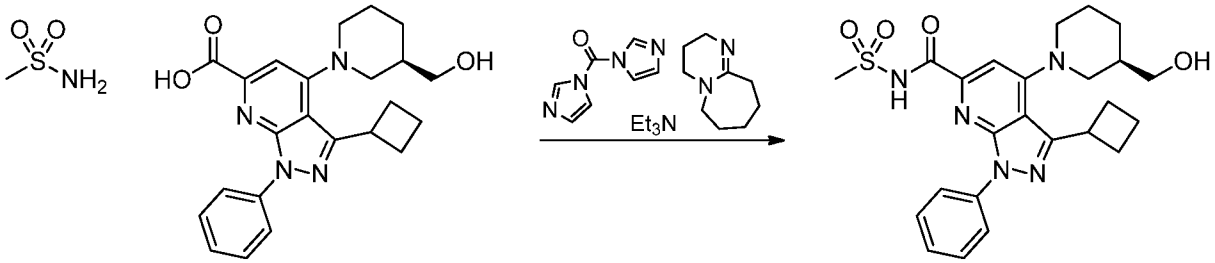
Illustrative synthesis of compound 347: 3-cyclobutyl-N-[3-(morpholin-4-yl)propane-1-sulfonyl]-4-[(oxan-4-yl)methoxy]-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



[00732] 3-Cyclobutyl-1-phenyl-4-(tetrahydropyran-4-ylmethoxy)pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (A148, 102 mg, 0.25 mmol) and carbonyl diimidazole (61 mg, 0.38 mmol) were stirred in anhydrous DMF (1.6 mL) at room temperature for one hour. Then a solution of 3-(morpholin-4-yl)propane-1-sulfonamide (S10, 104 mg, 0.50 mmol) in DMF (0.4 mL) and triethylamine (70 μL, 0.50 mmol) were added, followed by slow, dropwise addition of DBU (56 μL, 0.37 mmol). The reaction mixture was stirred for another thirty minutes, diluted with water

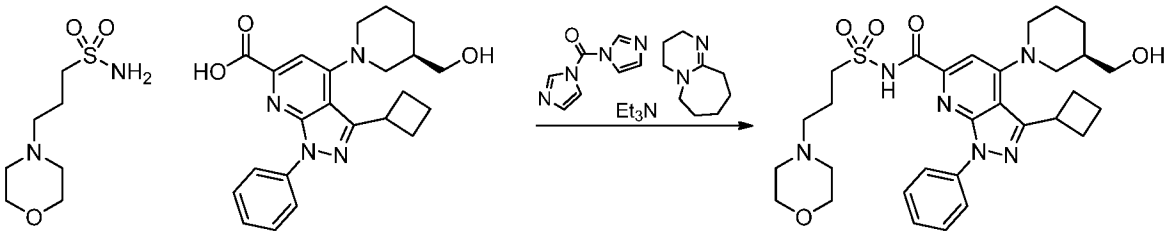
(8 mL), concentrated and purified by preparative HPLC on a Waters® Atlantis® T3 column (30 mm × 100 mm) with a 30 to 60% gradient of acetonitrile in 10 mM aqueous ammonium acetate at 50 mL/min to give the titled compound (61 mg).

Illustrative synthesis of compound 349: 3-cyclobutyl-4-[(3R)-3-(hydroxymethyl)piperidin-1-yl]-N-(methanesulfonyl)-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



[00733] 3-Cyclobutyl-4-[(3*R*)-3-(hydroxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (A284, 57 mg, 0.14 mmol) and carbonyl diimidazole (46 mg, 0.28 mmol) were stirred in anhydrous DMF (1.0 mL) at room temperature for about one hour. Then methanesulfonamide (27 mg, 0.28 mmol) and triethylamine (39 μL, 0.28 mmol) were added, followed by slow, dropwise addition of DBU (31.5 μL, 0.21 mmol). The reaction mixture was stirred more than 30 minutes, diluted with water (8 mL), concentrated and purified by preparative HPLC on a Waters® Atlantis® T3 C18 column (30 × 150 mm) with a 30 to 60% gradient of acetonitrile in 10 mM aqueous ammonium acetate at 50 mL/min to give the titled compound (17 mg).

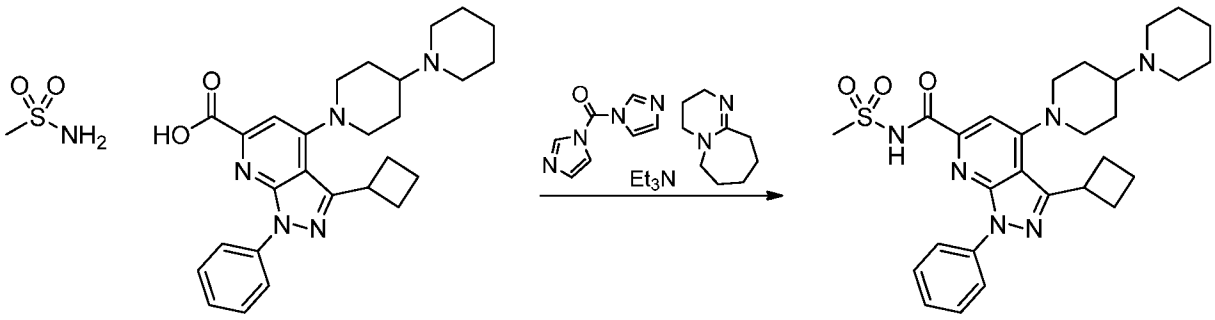
Illustrative synthesis of compound 350: 3-cyclobutyl-4-[(3R)-3-(hydroxymethyl)piperidin-1-yl]-N-[3-(morpholin-4-yl)propane-1-sulfonyl]-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



[00734] 3-Cyclobutyl-4-[(3*R*)-3-(hydroxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (A284, 61 mg, 0.15 mmol) and carbonyl diimidazole (49 mg, 0.30 mmol) were stirred in anhydrous DMF (1.0 mL) at room temperature for about one hour. Then a

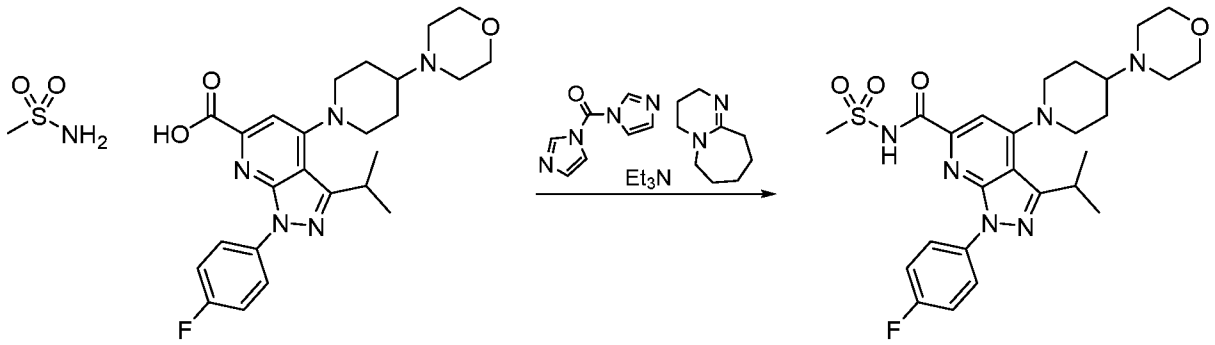
solution of 3-(morpholin-4-yl)propane-1-sulfonamide (S10, 63 mg, 0.30 mmol) in anhydrous acetonitrile (200 μL) and triethylamine (42 μL, 0.30 mmol) were added, followed by slow, dropwise addition of DBU (34 μL, 0.23 mmol). The reaction mixture was stirred for more than 30 minutes, diluted with water (8 mL), concentrated and purified by preparative HPLC on a Waters® Atlantis® T3 C18 column (30 × 150 mm) with a 40 to 70% gradient of acetonitrile in 10 mM aqueous ammonium acetate at 50 mL/min to the titled compound (30 mg).

Illustrative synthesis of compound 365: 4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-N-(methanesulfonyl)-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



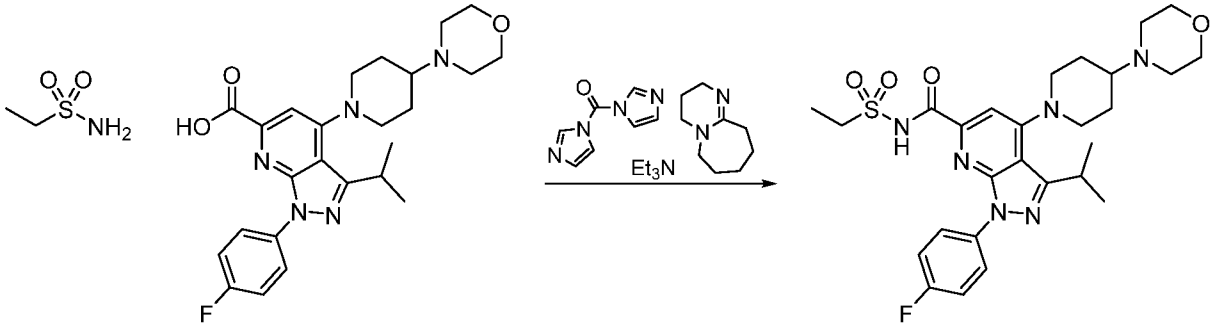
[00735] 3-Cyclobutyl-1-phenyl-4-[4-(1-piperidyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (A081, 51 mg, 0.11 mmol) and carbonyl diimidazole (28 mg, 0.17 mmol) were stirred in anhydrous DMF (600 μL) at room temperature for an hour. Then methanesulfonamide (21 mg, 0.22 mmol) and triethylamine (31 μL, 0.22 mmol) were added, followed by DBU (25.5 μL, 0.17 mmol). The reaction mixture was stirred 30 minutes at room temperature, diluted with water (5 mL), concentrated and purified by preparative HPLC on a Waters® Sunfire™ C8 column (30 × 150 mm) with a 30 to 60% gradient of acetonitrile in 10 mM aqueous ammonium acetate at 50 mL/min to give the titled compound (30 mg).

Illustrative synthesis of compound 411: 1-(4-fluorophenyl)-N-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-3-(propan-2-yl)-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



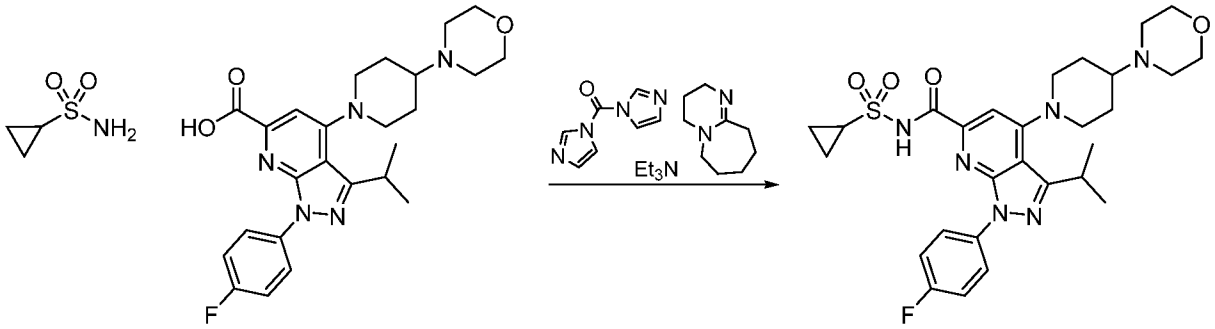
[00736] 1-(4-Fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (A408, 70 mg, 0.15 mmol) and carbonyl diimidazole (37 mg, 0.23 mmol) were stirred in anhydrous DMF (800 µL) at room temperature for an hour. Then methanesulfonamide (29 mg, 0.30 mmol) and triethylamine (42 µL, 0.30 mmol) were added, followed by slow addition of DBU (34 µL, 0.23 mmol). The reaction mixture was stirred 30 minutes at room temperature, diluted with methanol and purified by preparative HPLC on a Waters® Sunfire™ C8 column (30 × 150 mm) with a 30 to 60% gradient of acetonitrile in 10 mM aqueous ammonium acetate to give the titled compound.

Illustrative synthesis of compound 413: N-(ethanesulfonyl)-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-3-(propan-2-yl)-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



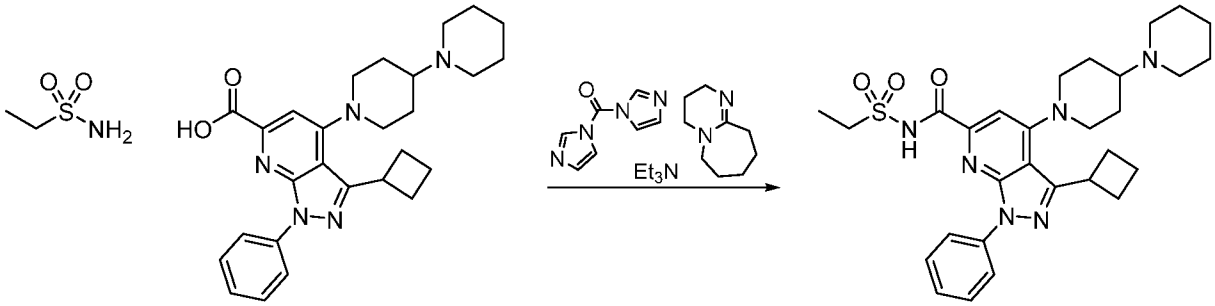
[00737] 1-(4-Fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (A408, 70 mg, 0.15 mmol) and carbonyl diimidazole (37 mg, 0.23 mmol) were stirred in anhydrous DMF (800 µL) at room temperature for an hour. Then ethanesulfonamide (33 mg, 0.30 mmol) and triethylamine (42 µL, 0.30 mmol) were added, followed by slow addition of DBU (34 µL, 0.23 mmol). The reaction mixture was stirred 30 minutes at room temperature, diluted with methanol and purified by preparative HPLC on a Waters® Sunfire™ C8 column (30 × 150 mm) with a 30 to 60% gradient of acetonitrile in 10 mM aqueous ammonium acetate to give the titled compound.

Illustrative synthesis of compound 414: N-(cyclopropanesulfonyl)-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-3-(propan-2-yl)-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



[00738] 1-(4-Fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (A408, 70 mg, 0.15 mmol) and carbonyl diimidazole (37 mg, 0.23 mmol) were stirred in anhydrous DMF (800 µL) at room temperature for an hour. Then cyclopropanesulfonamide (36 mg, 0.30 mmol) and triethylamine (42 µL, 0.30 mmol) were added, followed by slow addition of DBU (34 µL, 0.23 mmol). The reaction mixture was stirred 30 minutes at room temperature, diluted with methanol and purified by preparative HPLC on a Waters® Sunfire™ C8 column (30 × 150 mm) with a 30 to 60% gradient of acetonitrile in 10 mM aqueous ammonium acetate to give the titled compound.

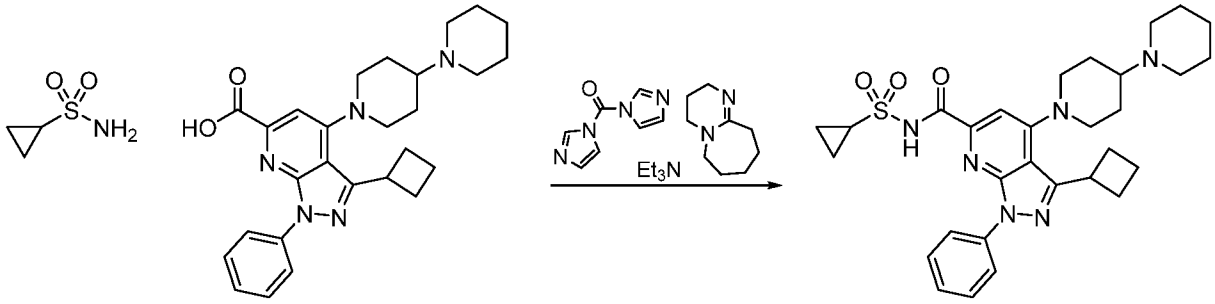
Illustrative synthesis of compound 427: 4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-N-(ethanesulfonyl)-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



[00739] 3-Cyclobutyl-1-phenyl-4-[4-(1-piperidyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (A081, 92 mg, 0.20 mmol) and carbonyl diimidazole (49 mg, 0.30 mmol) were stirred in anhydrous DMF (1.0 mL) at room temperature for 90 minutes. Then ethanesulfonamide (44 mg, 0.40 mmol) and triethylamine (56 µL, 0.40 mmol) were added, followed nearly 15 minutes later by slow addition DBU (45 µL, 0.30 mmol). The reaction

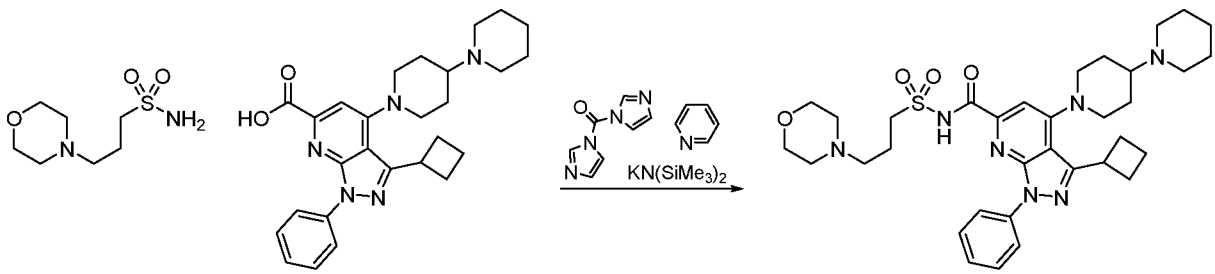
mixture was stirred 30 minutes at room temperature, diluted with methanol and purified by preparative HPLC on a Waters® Sunfire™ C8 column (30 × 150 mm) with a 40 to 70% gradient of acetonitrile in 10 mM aqueous ammonium acetate to give the titled compound.

Illustrative synthesis of compound 428: 4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-N-(cyclopropanesulfonyl)-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



[00740] 3-Cyclobutyl-1-phenyl-4-[4-(1-piperidyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (A081, 92 mg, 0.20 mmol) and carbonyl diimidazole (49 mg, 0.30 mmol) were stirred in anhydrous DMF (1.0 mL) at room temperature for 90 minutes. Then cyclopropanesulfonamide (49 mg, 0.40 mmol) and triethylamine (56 μL, 0.40 mmol) were added, followed nearly 15 minutes later by slow addition DBU (45 μL, 0.30 mmol). The reaction mixture was stirred 30 minutes at room temperature, diluted with methanol and purified by preparative HPLC on a Waters® Sunfire™ C8 column (30 × 150 mm) with a 30 to 60% gradient of acetonitrile in 10 mM aqueous ammonium acetate to give the titled compound.

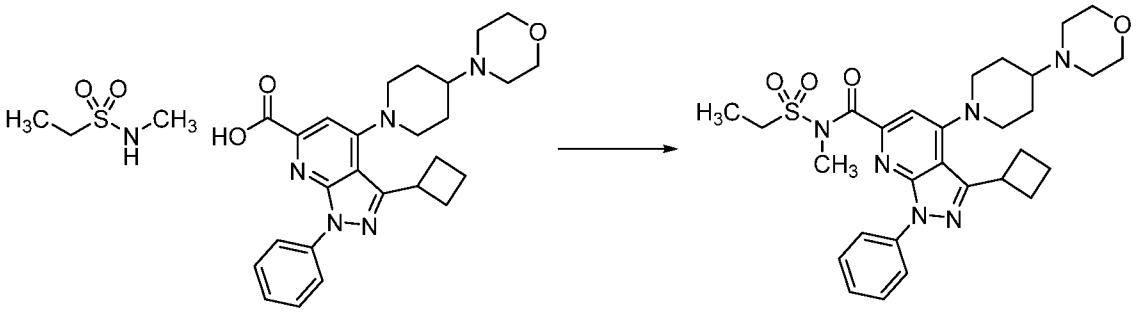
Illustrative synthesis of compound 454: 4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-N-[3-(morpholin-4-yl)propane-1-sulfonyl]-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



[00741] To a suspension of the 3-cyclobutyl-1-phenyl-4-[4-(1-piperidyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (46 mg, 0.10 mmol, A081) and carbonyl diimidazole (29 mg, 0.18 mmol) in anhydrous DMF (400 μL) was added pyridine (81 μL, 1.0 mmol). The mixture was stirred nearly ten minutes at room temperature and then another 15

minutes at 50 °C before being brought to room temperature. In a separate vial, 3-morpholinopropane-1-sulfonamide (42 mg, 0.20 mmol) under nitrogen was dissolved into anhydrous DMF (400 µL) and treated with 1 M potassium bis(trimethylsilyl)amide in THF (190 µL, 0.19 mmol), stirred ten minutes to give a suspension and then treated dropwise with the contents of the first vial, which were transferred with a DMF (200 µL) rinse. The mixture was stirred at room temperature for three days, diluted with methanol and purified by preparative HPLC on a Waters® Sunfire™ C8 column (30 × 150 mm) with a 35 to 65% gradient of acetonitrile in 10 mM aqueous ammonium acetate to give the titled compound.

Illustrative synthesis of compound 658: 3-cyclobutyl-N-(ethanesulfonyl)-N-methyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxamide

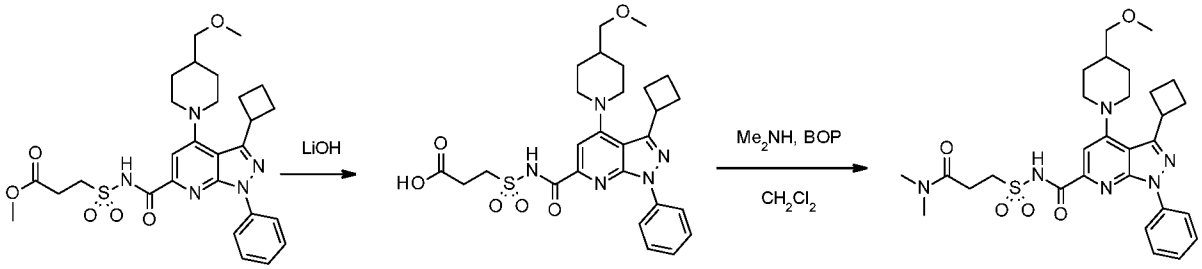


[00742] 3-Cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (45 mg, 0.10 mmol, A409) dissolved in dichloromethane (500 µL) was treated with 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (18 mg, 0.12 mmol) in dichloromethane (500 µL), dimethyl amino pyridine (24 mg, 0.2 mmol) and N-methylethanesulfonamide (13 mg, 0.11 mmol). The mixture was then stirred at room temperature overnight. The mixture was concentrated, and the residue was dissolved DMSO and purified by reverse phase HPLC (C18, 0-100% CH_3CN/water (0.1% TFA)). A gradient of acetonitrile (A) and 0.1% trifluoroacetic acid in water (B) was used, at a flow rate of 50mL/minute (0-0.5 minute 10% A, 0.5-6.0 minutes linear gradient 10-100% A, 6.0-7.0 minutes 100% A, 7.0-8.0 minutes linear gradient 100-10% A) gave the titled compound.

Method Y2: Synthesis of acylsulfonamide

Synthesis of compounds 289 & 298: 3-({3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carbonyl}sulfamoyl)propanoic acid and *3-cyclobutyl-N-[3-*

(dimethylamino)-3-oxopropane-1-sulfonyl]-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



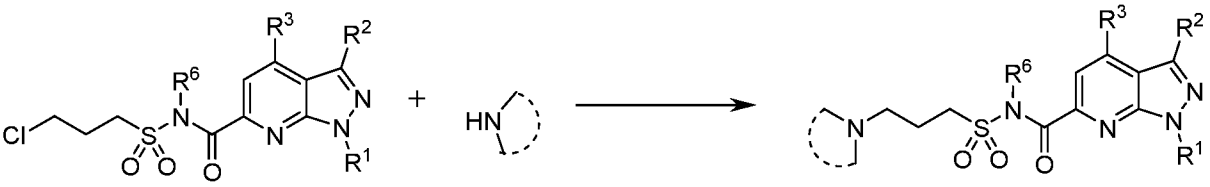
[00743] *Step 1: 3-({3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carbonyl}sulfamoyl)propanoic acid*

[00744] A solution of LiOH (0.0189 g, 0.45 mmol, 2.1 equiv) in H_2O (1 mL) was added to a solution of compound 288 (0.123 g, 0.216 mmol) in THF. The reaction mixture was stirred for 30 min and then concentrated. The residue was partitioned between dichloromethane (100 mL) and an aqueous H_3PO_4/NaH_2PO_4 buffer (1.0 M, pH 2, 100 mL). The organic phase was washed with brine, dried over $MgSO_4$, filtered and concentrated to give compound 289 (carboxylic acid).

[00745] *Step 2: 3-cyclobutyl-N-[3-(dimethylamino)-3-oxopropane-1-sulfonyl]-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxamide*

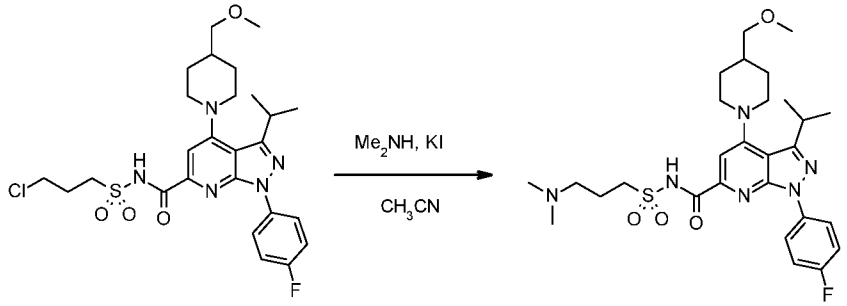
[00746] BOP (CAS: 56602-33-6, 0.037 g, 0.084 mmol, 1.2 equiv) was added to a solution of compound 289 (0.0378 g, 0.0680 mmol) in dichloromethane (4 mL). After 10 minutes, a THF solution of dimethylamine (2.0 M, 0.25 mL, 0.50 mmol, 7.3 equiv) was added. The reaction mixture was stirred at room temperature for 16 hours. The reaction mixture was charged onto a column of silica gel and eluted with CH_2Cl_2/iPrOH (20:1) to yield the titled compound. ^1H NMR (400 MHz, $CDCl_3/CD_3OD$) δ ppm 7.99 (d, J=8.25, 2H), 7.51 (t, J=8.0 Hz, 2H), 7.44 (s, 1H), 7.32 (t, J=7.4, 1H), 3.98 (pent, J=8.4 Hz, 1H), 3.67-3.59 (m, 2H), 3.50 (t, J=6.5 Hz, 2H), 3.40-3.33 (m, 2H), 3.37 (s, 3H), 3.14 (t, J=6.5 Hz, 2H), 2.94-2.84 (m, 2H), 2.6-2.49 (m, 2H), 2.44-2.34 (m, 2H), 2.38 (s, 6H), 2.12-1.79 (m, 5H), 1.60-1.48 (m, 2H)

Method Y3: Synthesis of acylsulfonamide



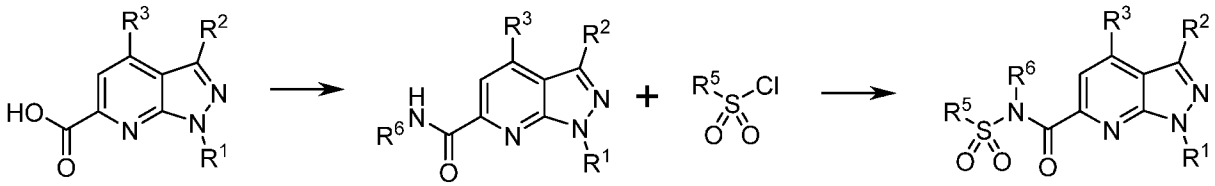
[00747] Potassium iodide (0.3 equiv) is added to a solution of alkylchloride in acetonitrile. The amine (15 to 20 equiv) is added, and the vial is sealed. The reaction mixture is stirred at RT or 50 °C for 16 hours. After concentration, the residue is partitioned between water and dichloromethane. The organic phase is washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. If necessary, the residue was purified either by precipitation in pentane or by silica gel chromatography.

Illustrative synthesis of compound 290: N-[3-(dimethylamino)propane-1-sulfonyl]-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



[00748] KI (2 mg, 0.012 mmol, 0.3 equiv) was added to a solution of *N*-(3-chloropropylsulfonyl)-1-(4-fluorophenyl)-3-isopropyl-4-[4-(methoxymethyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxamide (AC01, 20 mg, 0.035 mmol) in acetonitrile (3 mL). The vial was sealed, and the reaction mixture was saturated with gaseous dimethylamine. The reaction mixture was stirred at RT for 16 hours. After concentration, the residue was partitioned between water and dichloromethane. The organic phase was washed with brine, dried over $MgSO_4$, filtered and concentrated to give the titled compound.

Method Y4: Synthesis via carboxamide

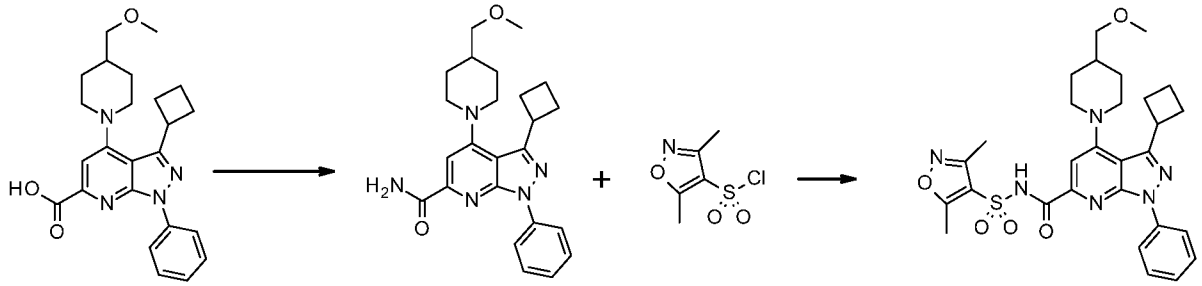


[00749] *Step 1*: Oxalyl chloride (0.40 mL, 4.7 mmol, 9.6 equiv) and a drop of dimethylformamide are added to a solution of carboxylic acid (0.49 mmol) in dichloromethane

(2 mL). After effervescence has ceased, the vial is sealed, and the reaction mixture is stirred at room temperature for 1 hour. The reaction mixture is concentrated in vacuo, and to the residue is added a dioxane solution of ammonia (0.5 M, 10.0 mL, 5.0 mmol, 10 equiv). After 1 hour, volatiles are then removed via rotary evaporation. The residue is purified by silica gel chromatography (dichloromethane/ethyl acetate, 4:1) to give the intermediate carboxamide.

[00750] *Step 2:* NaH (60% in mineral oil, 21 equiv to 50 equiv) is added to a solution of carboxamide in dry THF. After effervescence has ceased, sulfonyl chloride (1.4 to 2.0 equiv) is added. The reaction mixture is stirred at room temperature for several hours. An aqueous solution of malate buffer (1.0 M sodium malate/disodium malate, pH 4.5, 4 mL) is slowly added. After 5 minutes, the mixture is combined with chloroform or dichloromethane and stirred. The organic phase is collected and concentrated in vacuo. The residue is purified by preparative HPLC or by flash column chromatography to give the titled compound.

Illustrative synthesis of compound 287: 3-cyclobutyl-N-(3,5-dimethyl-1,2-oxazole-4-sulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxamide

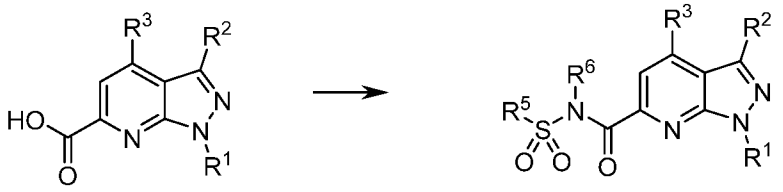


[00751] *Step 1*: Oxalyl chloride (0.40 mL, 4.7 mmol, 9.6 equiv) and a drop of dimethylformamide were added to a solution of A136 (0.207 g, 0.49 mmol) in dichloromethane (2 mL). After effervescence had ceased, the vial was sealed, and the reaction mixture was stirred at room temperature for 1 hour. The reaction mixture was concentrated, and to the residue was added a dioxane solution of ammonia (0.5M, 10.0 mL, 5.0 mmol, 10 equiv). After 1 hour, volatiles were then removed via rotary evaporation. The residue was purified by silica gel chromatography (CH_2Cl_2/EtOAc, 4:1) to give 3-cyclobutyl-4-[4-(methoxymethyl)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxamide.

[00752] *Step 2:* NaH (60% in mineral oil, 0.080 g, 2.0 mmol, 21 equiv) was added to a solution of 3-cyclobutyl-4-[4-(methoxymethyl)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-

carboxamide (0.041 g, 0.098 mmol) in dry THF (2 mL). After effervescence has ceased, 3,5-dimethylisoxazole-4-sulfonyl chloride (CAS: 877861-76-2, 0.038 g, 0.19 mmol, 1.9 equiv) was added. The reaction mixture was stirred at room temperature for 16 h. An aqueous solution of malate buffer (1.0 M sodium malate/disodium malate, pH 4.5, 4 mL) was slowly added. After 5 minutes, the mixture was combined with chloroform and agitated. The organic phase was collected and concentrated in vacuo. The residue was purified by preparative HPLC to give the titled compound.

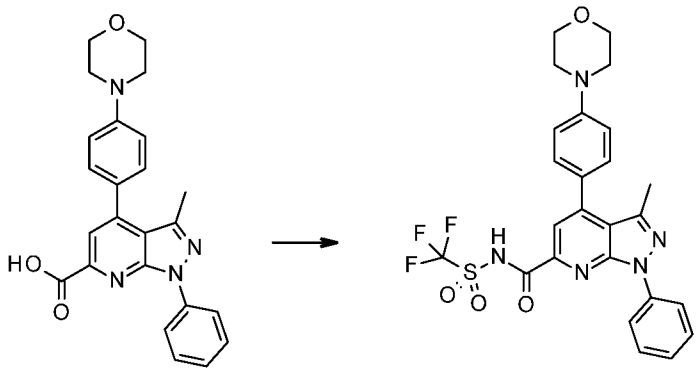
Method Y5: Synthesis of acylsulfonamide or acylsulfamide from a carboxylic acid chloride



[00753] Oxalyl chloride (CAS 79-37-8, 1.5 equiv) and 3 drops of dimethylformamide are added at 0 °C to a solution of carboxylic acid in dichloromethane. After 1 h of stirring at room temperature, additional oxalyl chloride (CAS 79-37-8, 1.5 equiv) is added. After 30 minutes of stirring, the reaction mixture is cooled to 0 °C and sulfonamide (3.0 equiv) followed by triethylamine (2.0 equiv) are added. The reaction mixture is stirred at room temperature for 3 h and then concentrated in vacuo. The residue is partitioned between a saturated aqueous solution of sodium hydrogencarbonate and dichloromethane. The organic phase is dried over $MgSO_4$, filtered and concentrated in vacuo. The residue dissolved in dichloromethane is precipitated by addition to a mixture of diethyl ether/pentane. The solid collected by filtration is purified by silica gel chromatography to give the titled compound.

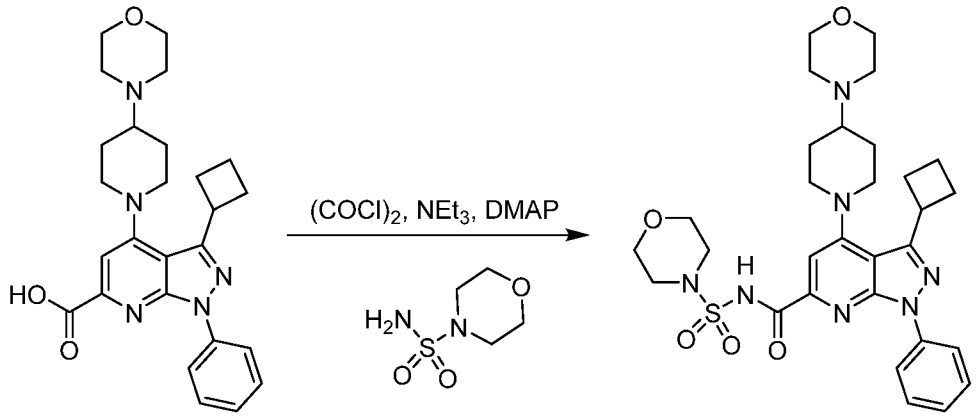
[00754] Alternatively, oxalyl chloride (5-10 equivalents) is added to a mixture of carboxylic acid (1 equiv) in dichloromethane followed by stirring at ambient temperature over 8-24 hours. The reaction mixture is diluted with dichloromethane and concentrated several times followed by drying under vacuum. The carboxylic acid chloride (1 equiv) is then combined with sulfonamide (2 equiv) and triethylamine (2.5-5 equiv) in dichloromethane with stirring at ambient temperature over 1-24 hours. The reaction mixture is concentrated and purified by preparative HPLC.

Illustrative synthesis of compound 3: 3-methyl-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-N-(trifluoromethanesulfonyl)-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



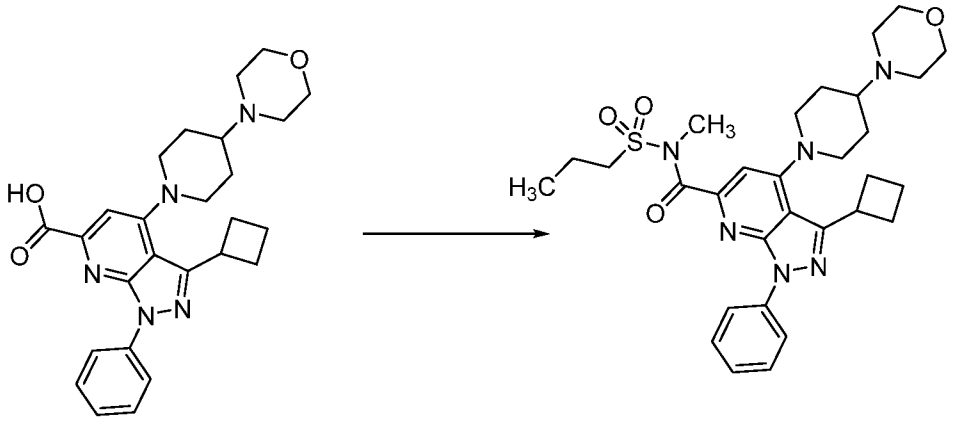
[00755] Oxalyl chloride (CAS 79-37-8, 0.012 mL, 0.15 mmol, 1.5 equiv) and 3 drops of dimethylformamide were added at 0 °C to a solution of A002 (41 mg, 0.1 mmol) in dichloromethane (2 mL). After 1 h of stirring at room temperature, additional oxalyl chloride (CAS 79-37-8, 0.012 mL, 0.15 mmol, 1.5 equiv) was added. After 30 minutes of stirring, the reaction mixture was cooled to 0 °C and trifluoromethanesulfonamide (CAS 421-85-2, 48 mg, 0.3 mmol, 3.0 equiv) followed by triethylamine (0.029 mL, 0.2 mmol, 2.0 equiv) were added. The reaction mixture was stirred at room temperature for 3 h and then concentrated in vacuo. The residue was partitioned between a saturated aqueous solution of sodium hydrogencarbonate and dichloromethane. The organic phase was dried over $MgSO_4$, filtered and concentrated. The residue dissolved in dichloromethane was precipitated by addition to a mixture of diethyl ether/pentane. The solid collected by filtration was purified by silica gel chromatography (heptane/EtOAc 100/0 to 0/100) to give the titled compound.

Illustrative synthesis of compound 383: 3-cyclobutyl-N-(morpholine-4-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



[00756] A suspension of 3-cyclobutyl-4-(4-morpholino-1-piperidyl)-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (A268, 0.0511 g, 0.111 mmol) and $(COCl)_2$ (18 µL, 0.206 mmol) in CH_2Cl_2 (0.40 mL) with catalytic DMF was stirred for 90 minutes, concentrated, and re-dissolved in CH_2Cl_2 (0.40 mL). To this mixture was added morpholine-4-sulfonamide (0.0213 g, 0.128 mmol), DMAP (0.0141 g, 0.115 mmol), and triethylamine (18 µL, 0.129 mmol), and the mixture was stirred overnight. The reaction mixture was then diluted with saturated $NaHCO_3$, extracted with CH_2Cl_2, concentrated, and chromatographed on silica gel (25% acetone/CH_2Cl_2) and re-chromatographed (2.5% CH_3OH/CH_2Cl_2) and precipitated (methanol/methyl *tert*-butyl ether) to give the titled compound (0.0267 g, 0.044 mmol, 40% yield).

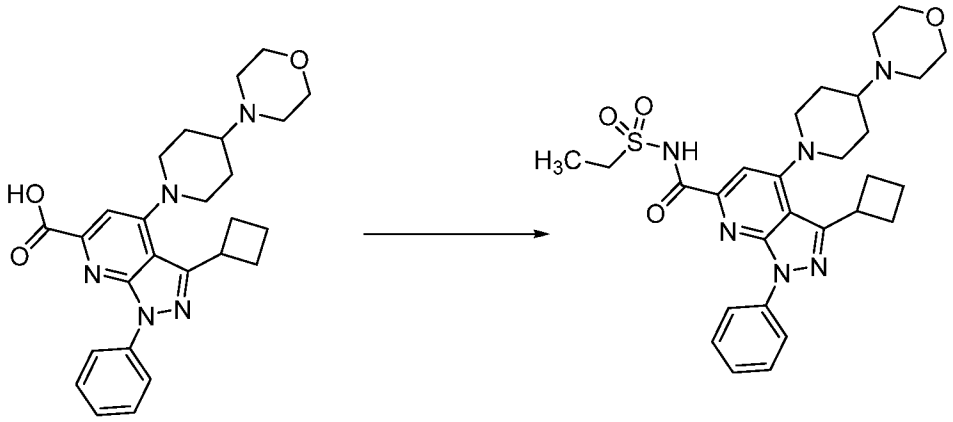
Illustrative synthesis of compound 432: 3-cyclobutyl-N-[methyl(propyl)sulfamoyl]-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



[00757] A vial was charged with 3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl chloride (35 mg, 0.08 mmol, prepared as described below for the synthesis of compound 437) dissolved in 500 µL of dichloromethane followed by

N-methyl-*N*-propylsulfonamide (2 eq, 0.15 mmol) in 500 μL of dichloromethane and neat triethylamine (38 μL, 4 eq, 0.32 mmol). The mixture was then stirred at room temperature for one hour. After completion of reaction, the mixture was concentrated, and the residue was dissolved in DMSO and purified by reverse phase HPLC (C18, 0-100% CH_3CN/water (0.1% TFA)). A gradient of acetonitrile (A) and 0.1% trifluoroacetic acid in water (B) was used, at a flow rate of 50mL/minute (0-0.5 minute 10% A, 0.5-6.0 minutes linear gradient 10-100% A, 6.0-7.0 minutes 100% A, 7.0-8.0 minutes linear gradient 100-10% A) to afford the title compound.

Illustrative synthesis of compound 437: *3-cyclobutyl-N-(ethanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxamide*



[00758] To a suspension of 3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (A409, 0.8117 g, 1.759 mmol) in dichloromethane (10 mL) was added oxalyl chloride (1 mL, 11.4 mmol) dropwise, and the mixture was stirred at RT overnight. The reaction mixture was diluted with more dichloromethane (11 mL) and concentrated under vacuum. This process was repeated two additional times. The resultant yellow solid material, which was kept under vacuum for one hour to give 3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl chloride.

[00759] To a suspension of 3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl chloride (0.050 g, 0.104 mmol) in dichloromethane (1.5 mL) was added ethanesulfonamide (0.023 g, 0.208 mmol) and triethylamine (0.051 mL, 0.365 mmol), and the mixture was stirred at RT for overnight. The reaction mixture was concentrated under vacuum and purified by preparative HPLC on a Waters® Sunfire™ C8 column (30 × 150 mm)

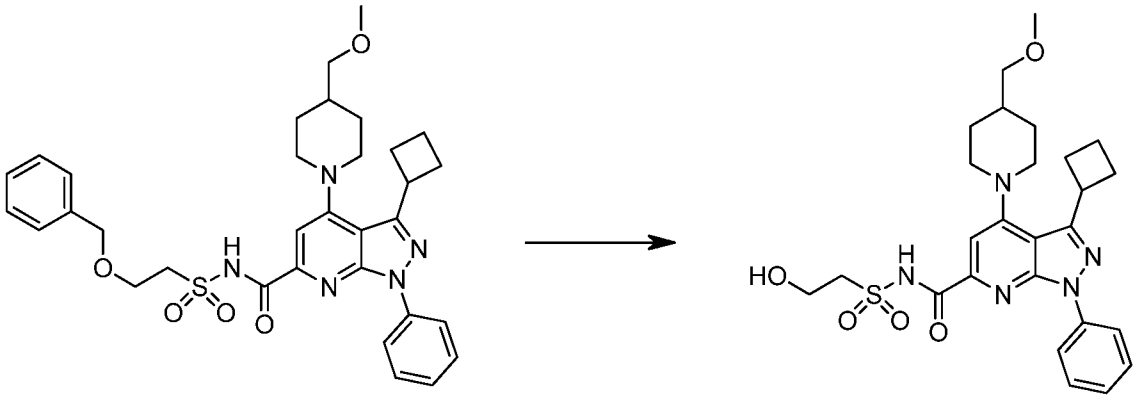
with an escalating gradient of acetonitrile in 10 mM aqueous ammonium acetate to the titled compound.

Method Y6: Protecting group removal

[00760] Protecting groups, known to one of skill in the art can be removed using appropriate procedures known to remove such protecting groups. Specific illustrations for select protecting group removal are provided in the examples below.

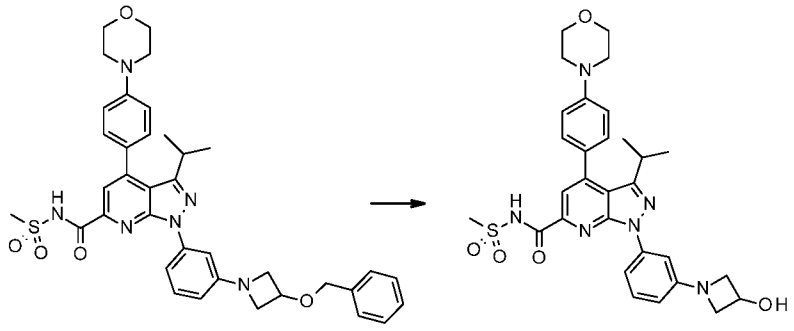
Benzyl ether removal

Illustrative synthesis of compound 366: 3-cyclobutyl-N-(2-hydroxyethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



[00761] A solution of AC05 (8 mg, 0.013 mmol) in THF (5 mL) was degassed with nitrogen. Palladium hydroxide (2 mg, 25% w/w) was added, and the reaction mixture was stirred under hydrogen atmosphere (balloon) for 3 hours. The reaction mixture was then filtered on Dicalite® diatomaceous earth, and the filtrate was concentrated in vacuo. The residue dissolved in dichloromethane (1 mL) was precipitated by addition to heptane. The collected solid was dried in vacuo to yield the titled compound.

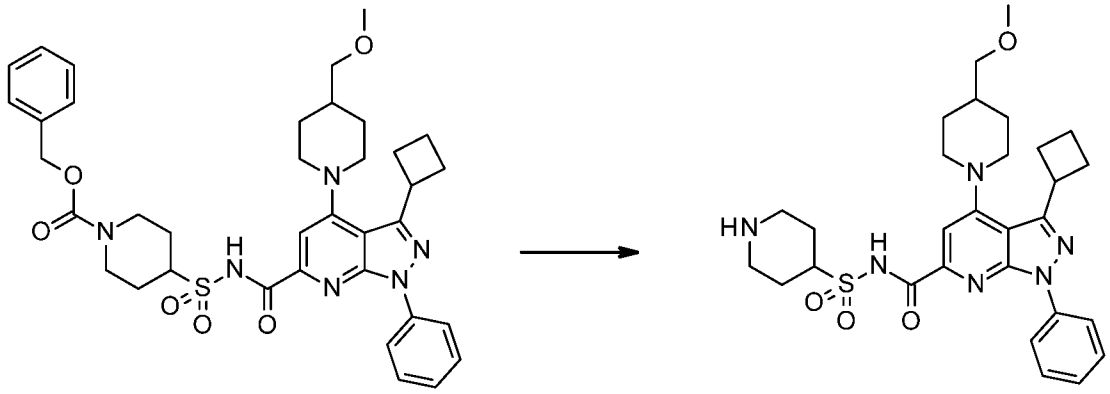
Illustrative synthesis of compound 105: 1-[3-(3-hydroxyazetidin-1-yl)phenyl]-N-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



[00762] A solution of AC02 (38 mg, 0.06 mmol) in a mixture of EtOH/THF (1/2 mL) was degassed with nitrogen. 10% Pd/C (5 mg) was added. The reaction mixture was degassed with H_2 for 5 min, and then was stirred for 48 hours at room temperature under hydrogen atmosphere (balloon). Additional 10% Pd/C (5 mg) was added, and the reaction mixture was stirred for 18 hours at room temperature under hydrogen atmosphere. The reaction mixture was filtered, and the filtrate was concentrated in vacuo. The residue was purified by preparative HPLC to give the titled compound.

Benzyl carbamate removal

Illustrative synthesis of compound 368: 3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-N-(piperidine-4-sulfonyl)-1H-pyrazolo[3,4-b]pyridine-6-carboxamide

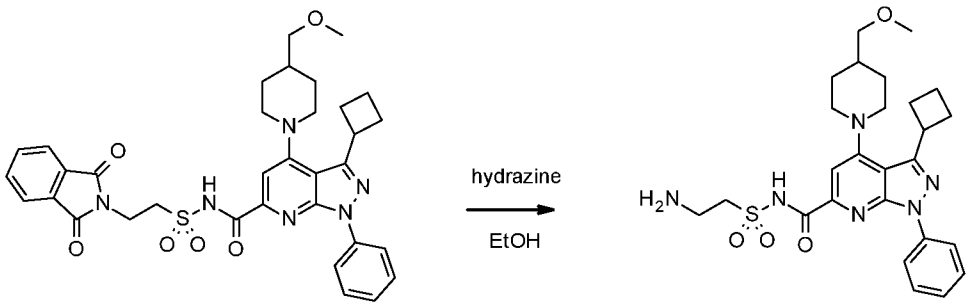


[00763] A solution of AC03 (60 mg, 0.09 mmol) in ethanol (10 mL) was degassed with nitrogen. Palladium hydroxide (15 mg, 25% w/w) was added, and the reaction mixture was stirred at RT under hydrogen atmosphere (balloon) for 16 hours. The reaction mixture was filtered, and the cake washed with THF, MeOH and chloroform. The filtrate was concentrated in

vacuo. The residue dissolved in dichloromethane was precipitated by addition to a mixture of diethyl ether and pentane. The obtained solid was dried in vacuo to yield the titled compound.

Phthalimide removal

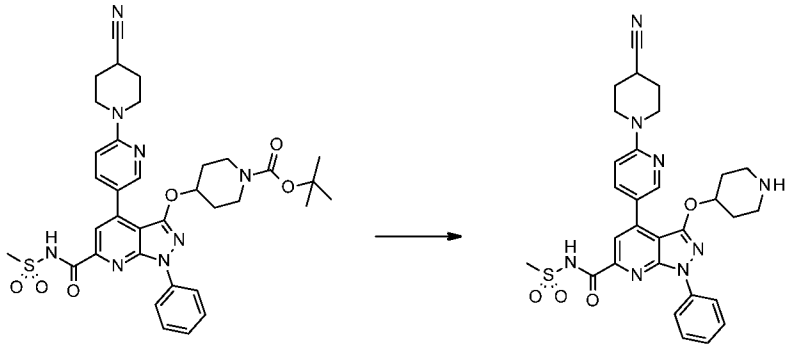
Illustrative synthesis of compound 261: N-(2-aminoethanesulfonyl)-3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



[00764] Hydrazine hydrate (50-60% in water, 0.015 mL, 0.2 mmol, 6.7 equiv) was added to a solution of 3-cyclobutyl-*N*-[2-(1,3-dioxoisoindolin-2-yl)ethylsulfonyl]-4-[4-(methoxymethyl)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxamide (compound 260, 20 mg, 0.03 mmol) in ethanol (3 mL). The reaction mixture was refluxed for 3 hours and then concentrated in vacuo. The residue was partitioned between a saturated aqueous solution of sodium hydrogencarbonate and dichloromethane. The organic phase was dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by silica gel chromatography (dichloromethane/acetone 95/5 to 85/15) to give the titled compound.

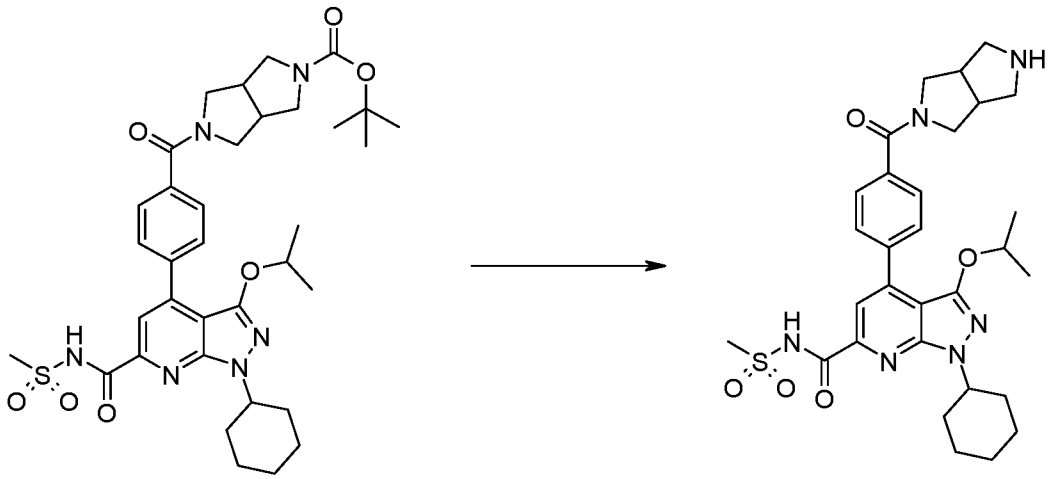
tert-Butyl carbamate removal

Illustrative synthesis of compound 258: 4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-N-(methanesulfonyl)-1-phenyl-3-[(piperidin-4-yl)oxy]-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



[00765] Trifluoroacetic acid (0.1 mL, 1.0 mmol, 23 equiv) was added to a solution of *tert*-butyl 4-[4-[6-(4-cyano-1-piperidyl)-3-pyridyl]-6-(methylsulfonylcarbamoyl)-1-phenyl-pyrazolo[3,4-*b*]pyridin-3-yl]oxypiperidine-1-carboxylate (compound 259, 30 mg, 0.043 mmol) in dichloromethane (1 mL). The reaction mixture was stirred at room temperature until completion of the reaction. The reaction mixture was quenched with a saturated solution of sodium bicarbonate. The obtained precipitate was collected by filtration, washed with water and dried to yield the titled compound.

Illustrative synthesis of compound 631: 1-cyclohexyl-4-[4-(hexahydropyrrolo[3,4-c]pyrrole-2(1H)-carbonyl)phenyl]-N-(methanesulfonyl)-3-[(propan-2-yl)oxy]-1H-pyrazolo[3,4-b]pyridine-6-carboxamide

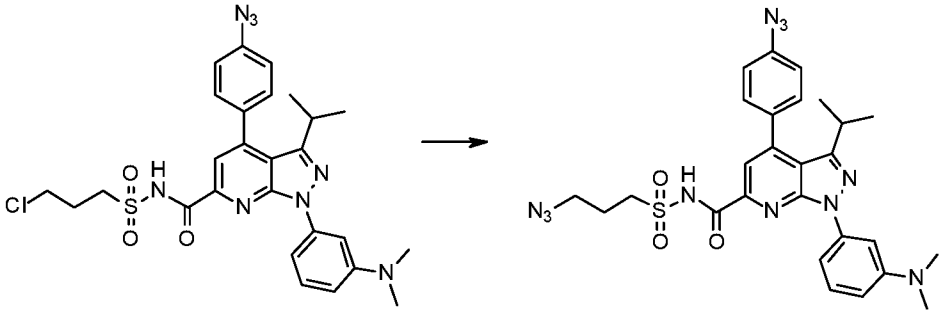


[00766] AC15 (18 mg, 26 µmol) was dissolved in dichloromethane (5 mL) and 4 M HCl in dioxane (0.5 mL, 2 mmol) was added. The solution was stirred at room temperature for two hours and then concentrated in vacuo. The residue was suspended in DCM and washed with a

phosphate buffer solution (pH 6.2). The organic phase was dried over sodium sulfate, filtered and concentrated under reduced pressure to give the titled compound.

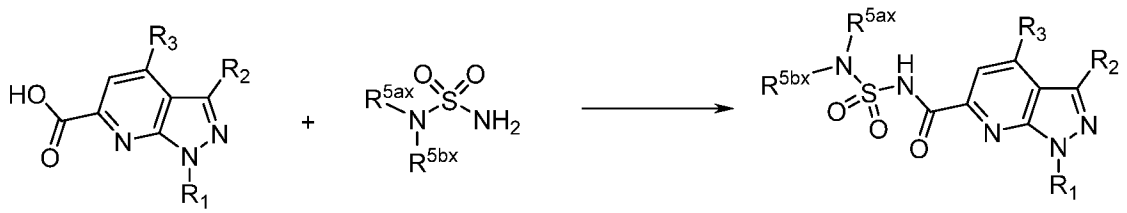
Method Y7: Azide displacement of alkyl halide

Synthesis of compound 327: 4-(4-azidophenyl)-N-(3-azidopropane-1-sulfonyl)-1-[3-(dimethylamino)phenyl]-3-(propan-2-yl)-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



[00767] AC06 (160 mg, 0.275 mmol, 1 equiv) in anhydrous DMSO (2 mL) at RT under nitrogen atmosphere was added sodium azide (CAS 26628-22-8, 36 mg, 0.550 mmol, 2.0 equiv). The reaction mixture was stirred at 80 °C for 1 h. Then the reaction mixture was cooled down, diluted with dichloromethane, washed with water and brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting crude mixture was purified by preparative HPLC to afford the titled compound.

Method Y8: Synthesis of acylsulfamide

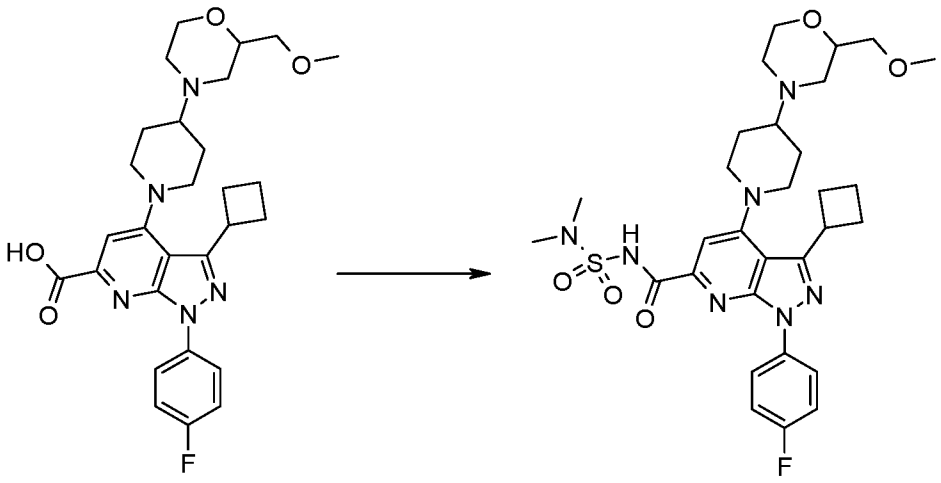


[00768] EDC•HCl (CAS 25952-538, 1.0 to 4.0 equiv) is added at RT to a stirring solution of carboxylic acid, sulfamide (from 1 to 4.0 equiv) and 4-(dimethylamino) pyridine (CAS 1122-58-3, from 0.2 to 2 equiv) in dichloromethane or/and THF or/and acetonitrile. The reaction mixture is stirred at RT until complete conversion. The solvent can be evaporated under reduced pressure. The residue can be worked up or purified by preparative HPLC. The work up consists in dissolving the sample in DCM and washing it with water and/or a saturated aqueous solution

of $NaHCO_3$. The organic phase is separated, dried over sodium sulfate, filtered and concentrated in vacuo. The residue is purified either by flash column chromatography or by preparative HPLC to yield the titled compound.

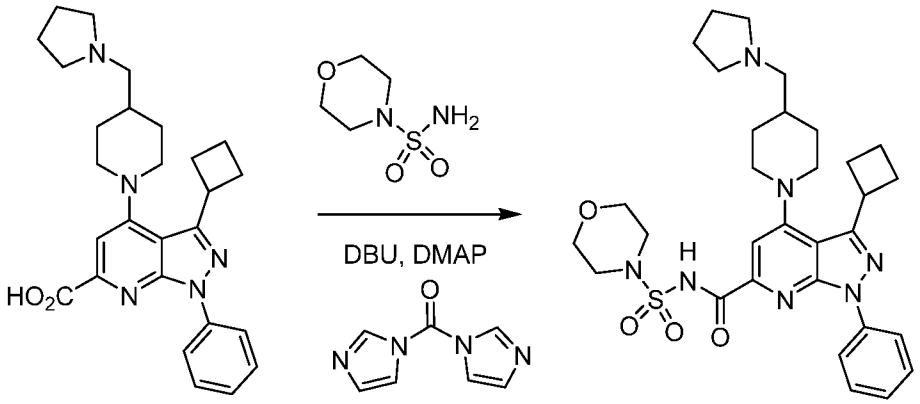
[00769] Alternatively, acylsulfamides can be prepared in the following manner. A solution of the carboxylic acid (1 eq) in dichloromethane, dichloroethane or dimethylformamide can be treated with carbodiimidazole (1-2.5 eq) stirred at ambient temperature to 65 °C for 0.5-3 hours. Then the sulfamide (1-3 eq) and optional potassium bis(trimethylsilyl)amide or triethylamine followed by 1,8-diazabicycloundec-7-ene (1-3 eq) and optional 4-(dimethylamino)pyridine (1-2 eq) can be added, and the reaction mixture is stirred at 20-60 °C for 2-16 hours. The reaction mixture can then be concentrated or extractively worked up. The residue can be purified by precipitation, silica gel flash chromatography, or preparative HPLC.

Illustrative synthesis of compound 379: 3-cyclobutyl-N-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[2-(methoxymethyl)morpholin-4-yl]piperidin-1-yl}-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



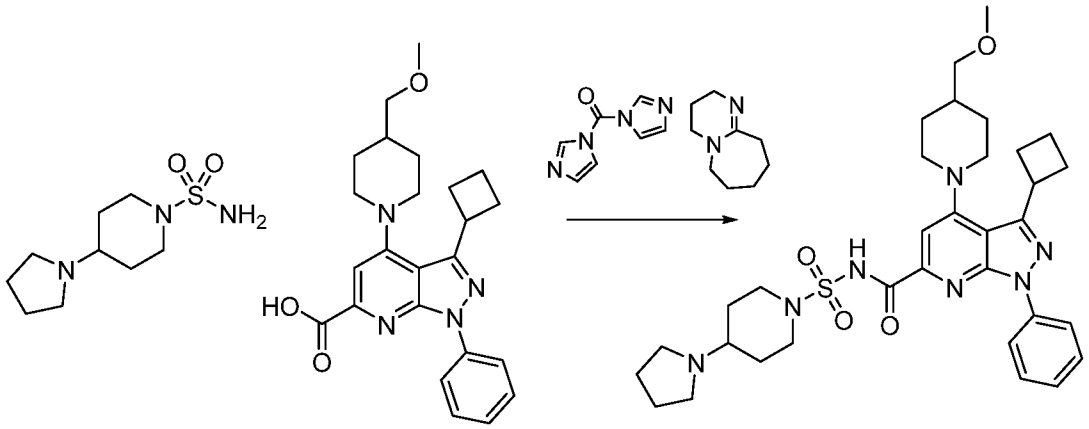
[00770] EDC•HCl ([25952-538], 58 mg, 0.46 mmol) was added at RT to a stirred solution of A286 (120 mg, 0.23 mmol), *N,N*-dimethylsulfamide (58 mg, 0.46 mmol) and 4-(dimethylamino) pyridine (CAS 1122-58-3, 58 mg, 0.46 mmol) in a mixture of dichloromethane/acetonitrile (1:1, 4 mL). The reaction mixture was stirred at RT for 20 hours. The solvent was evaporated at 40 °C under a nitrogen flow. The residue was purified by preparative HPLC to yield the titled compound as formate salt.

Illustrative synthesis of compound 380: 3-cyclobutyl-N-(morpholine-4-sulfonyl)-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



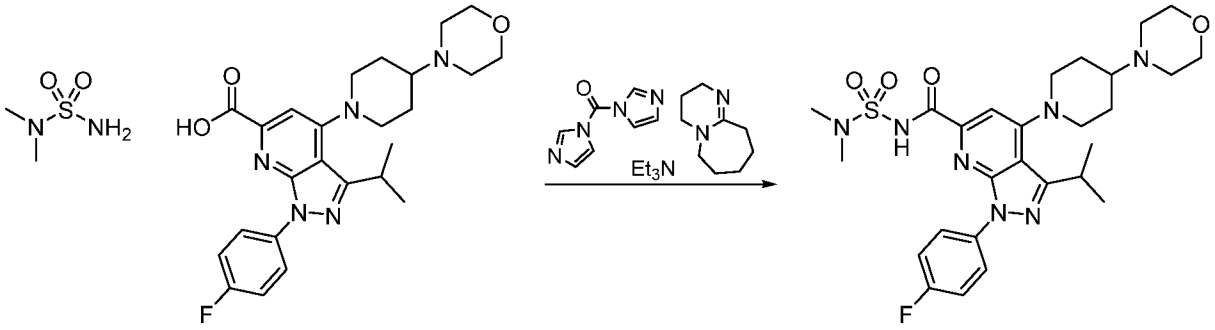
[00771] A suspension of 3-cyclobutyl-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (A285, 0.1498 g, 0.326 mmol) and carbonyl diimidazole (0.0795 g, 0.490 mmol) in dimethylformamide (DMF) (1.0 mL) was stirred for 2.5 hours, and then morpholine-4-sulfonamide (0.0815 g, 0.490 mmol, [25999-04-6]), DMAP (0.0444 g, 0.363 mmol), and DBU (0.075 mL, 0.498 mmol) were added. The resultant mixture was stirred overnight. The reaction mixture was then diluted with water (10 mL), extracted with dichloromethane (3 × 8 mL), dried (Na_2SO_4), and chromatographed (7% CH_3OH/CH_2Cl_2) and triturated (10 volumes methyl *tert*-butyl ether/5 volumes methanol) to give the titled compound (0.0602 g, 0.099 mmol, 30% yield).

Illustrative synthesis of compound 388: 3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-N-[4-(pyrrolidin-1-yl)piperidine-1-sulfonyl]-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



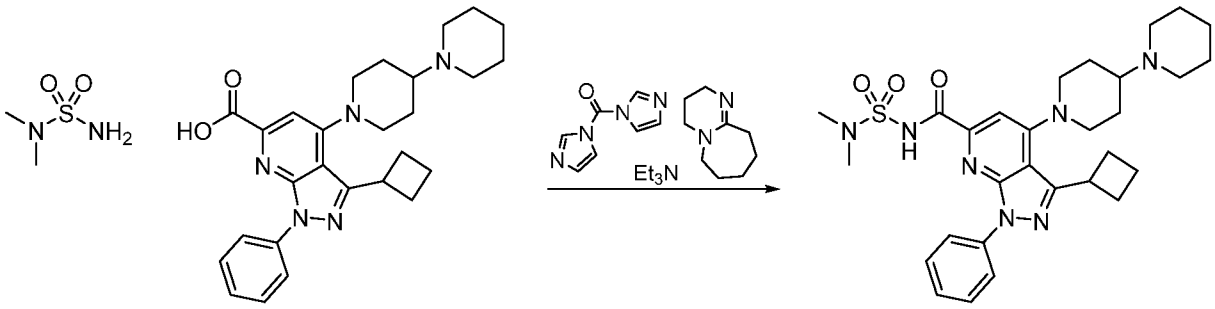
[00772] A 4-mL vial was charged with 3-cyclobutyl-4-[4-(methoxymethyl)-1-piperidyl]-1-phenyl-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (A136, 35 mg, 0.09 mmol) dissolved in 600 μL of dichloroethane followed by carbonyldiimidazole (27 mg, 0.18 mmol) in 600 μL of dichloroethane, and the mixture was stirred at 40 °C for two hours. To this mixture was then added 4-(pyrrolidin-1-yl)piperidine-1-sulfonamide (40 mg, 3 eq, 0.28 mmol) followed by 1,8-diazabicycloundec-7-ene (42 μL, 3eq, 0.28 mmol), and the mixture was heated at 60 °C for 16 hours. The mixture was concentrated, and the residue was dissolved in DMSO and purified by reverse phase HPLC (C18, 0-100% CH_3CN/water (0.1% TFA)). A gradient of acetonitrile (A) and 0.1% trifluoroacetic acid in water (B) was used, at a flow rate of 50 mL/minute (0-0.5 minute 10% A, 0.5-6.0 minutes linear gradient 10-100% A, 6.0-7.0 minutes 100% A, 7.0-8.0 minutes linear gradient 100-10% A) to afford the title compound.

Illustrative synthesis of compound 412: N-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-3-(propan-2-yl)-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



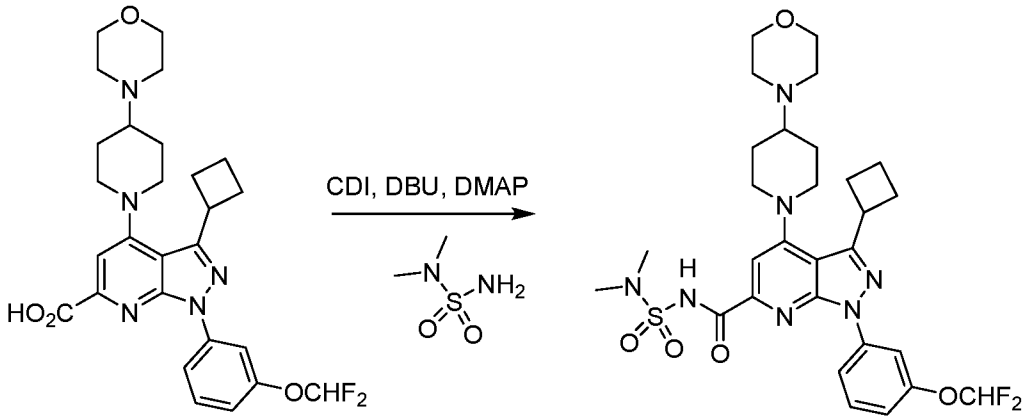
[00773] 1-(4-Fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (A408, 70 mg, 0.15 mmol) and carbonyl diimidazole (37 mg, 0.23 mmol) were stirred in anhydrous DMF (800 μL) at room temperature for an hour. Then *N,N*-dimethylsulfamide (37 mg, 0.30 mmol) and triethylamine (42 μL, 0.30 mmol) were added, followed by slow addition of DBU (34 μL, 0.23 mmol). The reaction mixture was stirred 30 minutes at room temperature, diluted with methanol and purified by preparative HPLC on a Waters® Sunfire™ C8 column (30 × 150 mm) with a 40 to 70% gradient of acetonitrile in 10 mM aqueous ammonium acetate to give the titled compound.

Illustrative synthesis of compound 426: 4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-N-(dimethylsulfamoyl)-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



[00774] 3-Cyclobutyl-1-phenyl-4-[4-(1-piperidyl)-1-piperidyl]pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (A081, 92 mg, 0.20 mmol) and carbonyl diimidazole (49 mg, 0.30 mmol) were stirred in anhydrous DMF (1.0 mL) at room temperature for 90 minutes. Then *N*,*N*-dimethylsulfamide (50 mg, 0.40 mmol) and triethylamine (56 µL, 0.40 mmol) were added, followed nearly 15 minutes later by slow addition DBU (45 µL, 0.30 mmol). The reaction mixture was stirred 30 minutes at room temperature, diluted with methanol and purified by preparative HPLC on a Waters® Sunfire™ C8 column (30 × 150 mm) with a 30 to 60% gradient of acetonitrile in 10 mM aqueous ammonium acetate to give the titled compound.

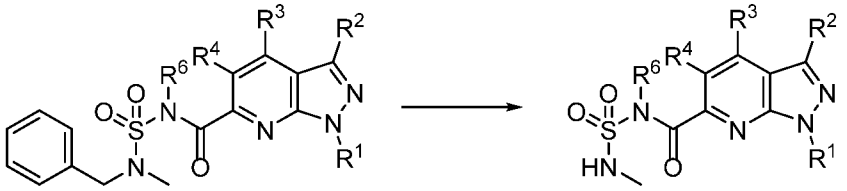
Illustrative synthesis of compound 652: 3-cyclobutyl-1-[3-(difluoromethoxy)phenyl]-N-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



[00775] A solution of 3-cyclobutyl-1-[3-(difluoromethoxy)phenyl]-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid (0.0536 g, 0.102 mmol, A410) and 1,1'-carbonyldiimidazole (0.0253 g, 0.156 mmol) in *N*,*N*-dimethylformamide (DMF) (0.40 mL) was stirred at 60 °C for 1 hour. Then *N*,*N*-dimethylsulfamide (0.0192 g, 0.155 mmol), DMAP (0.0138 g, 0.113 mmol), and DBU (0.023 mL, 0.153 mmol) were added, and the mixture

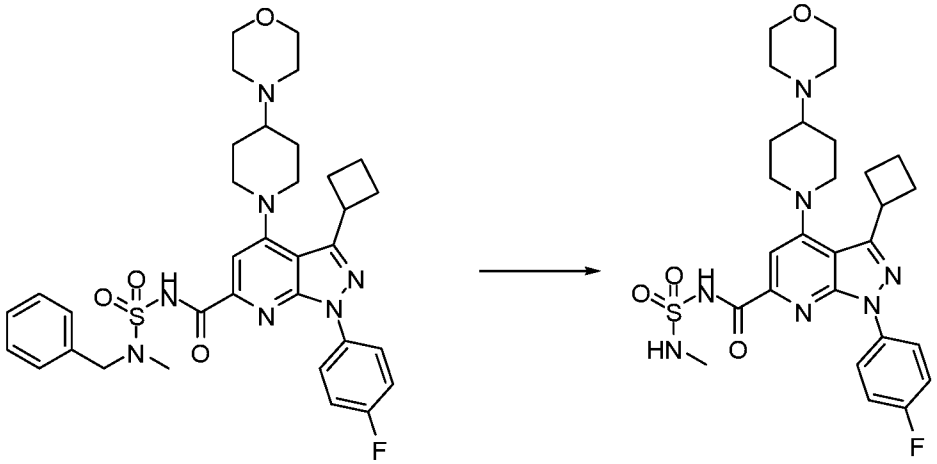
was stirred for 2.5 hours. The mixture was diluted with water (10 mL), extracted with DCM (4x8 mL), dried (Na_2SO_4), and concentrated. The residue was purified by chromatography on silica gel (0-3% isopropanol/DCM) to give the titled compound

Method Y9: De-benzylation



[00776] A vial is loaded with benzylated acylsulfonamide (1.0 equiv) and 10% Pd on charcoal (0.1 equiv). The vial is sealed, evacuated and back-filled with N_2 and THF/MeOH 1:1 is added by syringe. The reaction mixture is evacuated and back-filled with H_2 three times, and the reaction mixture is stirred overnight at 50 °C. The mixture is filtered on a Pall-Seitz thick paper filter and concentrated in vacuo. The residue is dissolved in MeOH, filtered over a 0.45 µM plug filter and purified by means of semi-preparative HPLC (0.1% TFA in water /CH_3CN). The compound is dissolved in DCM, 4 M HCl in dioxane is added, and the mixture was concentrated in vacuo to afford the debenzylated compound.

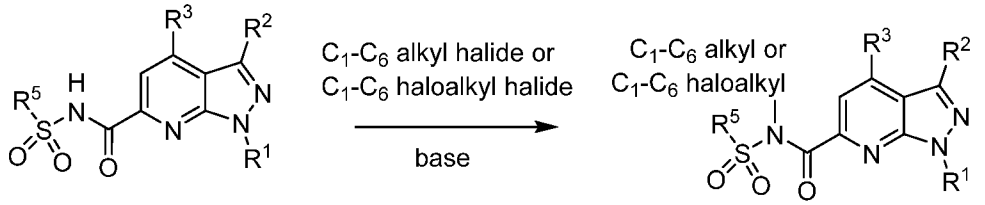
Illustrative synthesis of compound 517: 3-cyclobutyl-1-(4-fluorophenyl)-N-(methylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



[00777] A vial was loaded with *N*-[benzyl(methyl)sulfamoyl]-3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide (AC16, 1.0 equiv., 0.151 mmol, 100 mg) and 10% Pd on charcoal (0.1 equiv., 0.015 mmol, 16

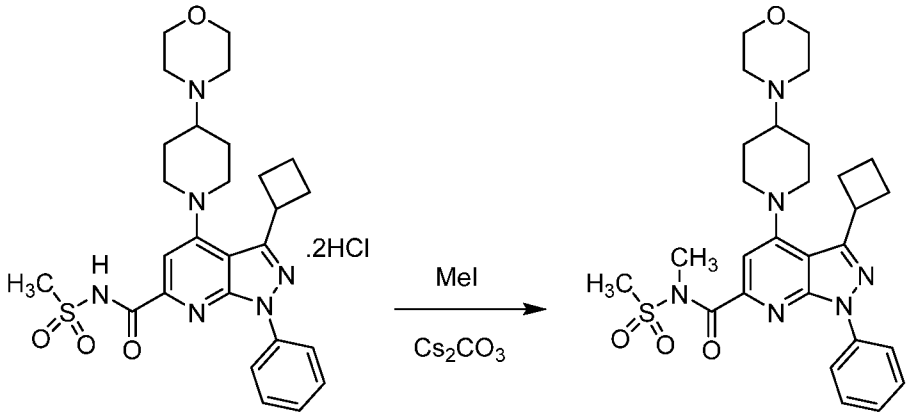
mg). The vial was sealed, evacuated and back-filled with N_2, and THF/MeOH 1:1 (2 mL) was added by syringe. The reaction mixture was evacuated and back-filled with H_2 three times, and the reaction mixture was stirred overnight at 50 °C. The mixture was filtered on a Pall-Seitz thick paper filter and concentrated in vacuo. The residue was dissolved in MeOH, filtered over a 0.45 µM plug filter and purified by means of semi-preparative HPLC (0.1% TFA in water/CH_3CN). The compound was dissolved in DCM, and then 4 M HCl in dioxane (0.1 mL) was added and the mixture was concentrated in vacuo to afford the titled compound.

Method Y10: Acylsulfonamide N-alkylation



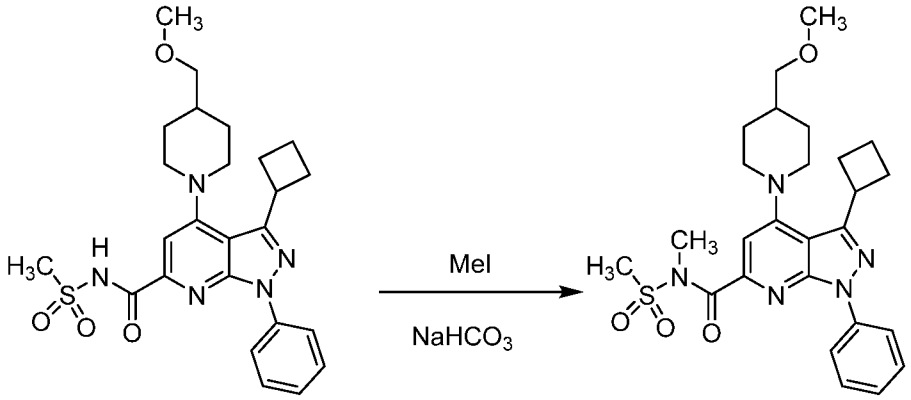
[00778] An acylsulfonamide is treated with a C_1-C_6 alkyl halide or C_1-C_6 alkyl halide in the presence of a base such as but not limited to sodium bicarbonate or cesium carbonate in acetonitrile or *N,N*-dimethylformamide or a mixture thereof at room temperature to 70 °C over 8-60 hours. The reaction mixture is optionally quenched with water. The mixture may be optionally extractively worked up and concentrated or simply concentrated. The residue can be purified by precipitation, chromatography on silica gel, or by preparative HPLC to give the N-alkylated acylsulfonamide.

Illustrative synthesis of compound 656: 3-cyclobutyl-N-(methanesulfonyl)-N-methyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



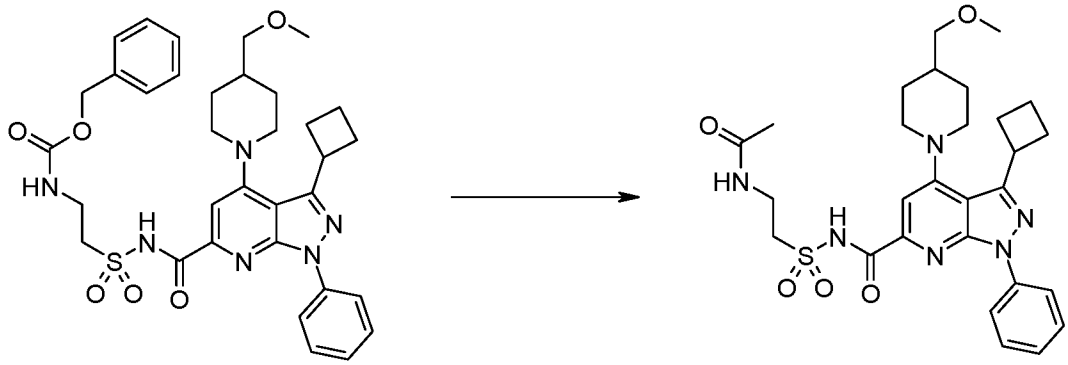
[00779] A mixture of 3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide dihydrochloride (0.0318 g, 0.052 mmol, compound 328), iodomethane (4.86 µl, 0.078 mmol), and Cs_2CO_3 (0.0506 g, 0.155 mmol) in *N*,*N*-dimethylformamide (DMF) (0.25 mL) was stirred at RT for 1 hour, and at 60 °C overnight. The mixture was then quenched with water, concentrated, and chromatographed on silica gel (5% MeOH/DCM) and re-chromatographed (15-25% acetone/DCM) to give the titled compound.

Illustrative synthesis of compound 657: 3-cyclobutyl-N-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-N-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxamide



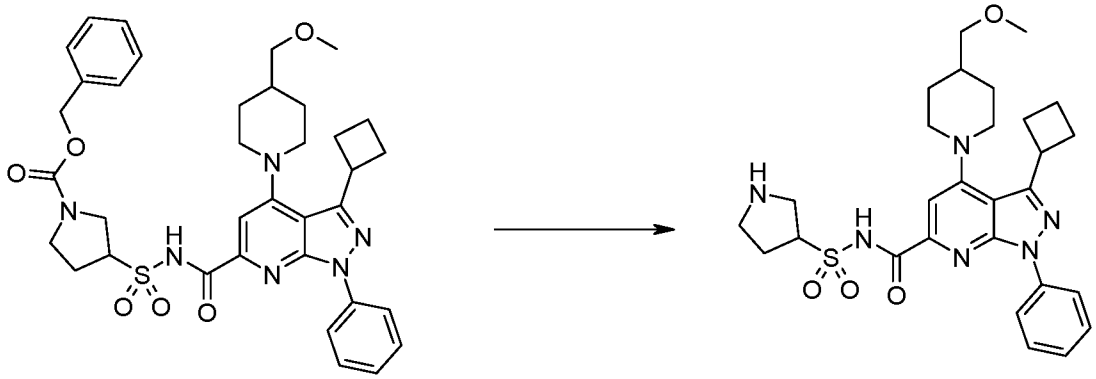
[00780] A mixture of 3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide (0.0508 g, 0.102 mmol, compound 185), iodomethane (10 µL, 0.161 mmol), and $NaHCO_3$ (0.0265 g, 0.315 mmol) in acetonitrile (0.40 mL) was stirred at RT overnight. *N*,*N*-Dimethylformamide (DMF) (0.20 mL) was added, and the mixture was heated to 60 °C for 5 hours (little reaction). Then, additional iodomethane (10 µL, 0.161 mmol) and $NaHCO_3$ (0.0265 g, 0.315 mmol) were added, and the mixture was stirred at 60 °C overnight. The mixture was diluted with water, extracted with DCM, dried (Na_2SO_4), and chromatographed on silica gel (2% EtOAc/DCM) to give the titled compound.

Synthesis of compound 386: *N*-(2-acetamidoethanesulfonyl)-3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-:



[00781] A solution of AC08 (42 mg, 0.06 mmol) in a mixture of THF (6 mL) and acetic anhydride (0.1 mL, 1.0 mmol) was degassed with nitrogen. 10% Pd/C (9 mg, 0.008 mmol) was added and the reaction mixture was purged with H_2. The mixture was stirred for 16 hours at RT under a hydrogen atmosphere (balloon). The reaction mixture was filtered over a pad of diatomaceous earth that was then washed with THF. The filtrate was concentrated in vacuo, and the residue was purified by flash column chromatography eluted with DCM/MeOH (20/1) to give the titled compound.

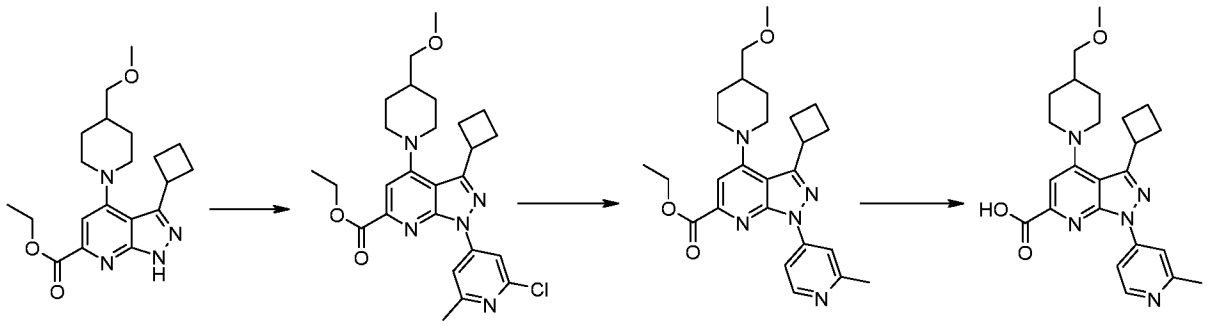
Synthesis of compound 387: 3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-*N*-(pyrrolidine-3-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide:



[00782] A solution of AC09 (103 mg, 0.15 mmol) in a mixture of THF(8 mL), ethanol (8 mL), acetic acid (1 mL), and aqueous 1 M HCl (1 mL) was degassed with nitrogen. 10% $Pd(OH)_2$ (21 mg, 0.015 mmol) was added, and the reaction mixture was purged with H_2. The mixture was stirred for 16 hours at RT under a hydrogen atmosphere (balloon). The reaction mixture was filtered over a pad of diatomaceous earth that was washed with THF. The filtrate and wash were concentrated in vacuo. The residue was partitioned between chloroform (100 mL) and aqueous 1 M NaOH (50 mL). The organic phase was dried over magnesium sulfate,

filtered and concentrated under reduced pressure. The residue was purified by silica gel chromatography eluted with DCM/MeOH (20/1) to give the titled compound.

Synthesis of AC10: 3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-(2-methylpyridin-4-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid:



[00783] *Step 1: ethyl 1-(2-chloro-6-methylpyridin-4-yl)-3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1H-pyrazolo[3,4-b]pyridine-6-carboxylate*

[00784] To a solution of E168 (64 mg, 0.17 mmol) in dichloromethane (4 mL) at RT was added 2-chloro-6-methylpyridine-4-boronic acid ([1320397-15-6], 43 mg, 0.25 mmol), copper(II) acetate ([142-71-2], 56 mg, 0.31 mmol) and pyridine (66 µL, 0.81 mmol). The reaction mixture was stirred at room temperature under air for 72 hours. The reaction mixture was filtered through a pad of diatomaceous earth. Solids were washed with dichloromethane, and the filtrate was concentrated in vacuo. The resulting residue was purified by flash chromatography on silica gel eluted with ethyl acetate/*n*-heptane (0/1 to 1/0) to give the titled compound.

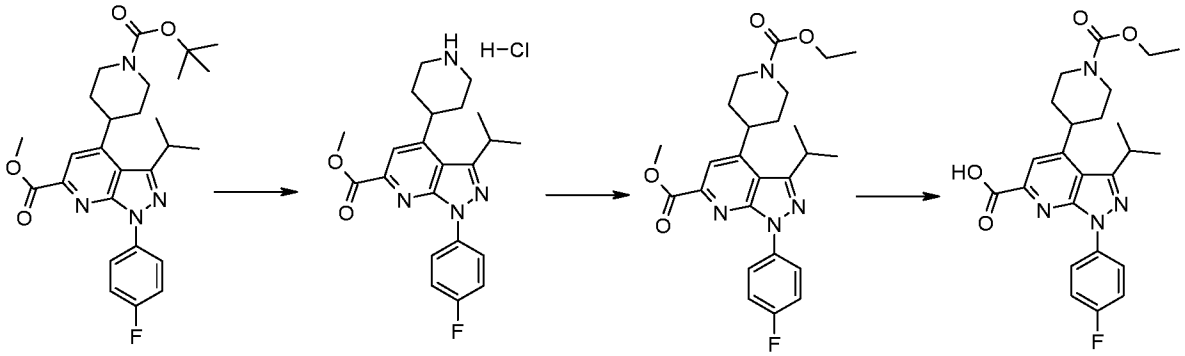
[00785] *Step 2: ethyl 3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-(2-methylpyridin-4-yl)-1H-pyrazolo[3,4-b]pyridine-6-carboxylate*

[00786] A solution of the compound from the previous step (50 mg, 0.1 mmol) in ethanol (20 mL) was degassed with nitrogen. 10% Pd/C (5 mg, 0.005 mmol) was added, and the reaction mixture was purged with H_2. The mixture was stirred for 16 hours at RT under a hydrogen atmosphere (balloon). The reaction mixture was filtered through a pad of diatomaceous earth that was washed with ethanol. The filtrate was concentrated in vacuo to give the titled compound.

[00787] *Step 3: 3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-(2-methylpyridin-4-yl)-1H-pyrazolo[3,4-b]pyridine-6-carboxylic acid*

[00788] The previous compound (50 mg, 0.1 mmol) was dissolved ethanol (5 mL), and aqueous 1 N sodium hydroxide (0.5 mL, 0.5 mmol) was added at RT. The solution was stirred for 16 hours. A phosphate buffer was added (pH 6.2). The solvent was partially removed under reduced pressure, and the resulting mixture was extracted twice with chloroform. The combined organic phases were dried over magnesium sulfate, filtered and concentrated under reduced pressure to give the titled compound.

Synthesis of AC13: 4-[1-(ethoxycarbonyl)piperidin-4-yl]-1-(4-fluorophenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid



[00789] *Step 1: methyl 1-(4-fluorophenyl)-4-(piperidin-4-yl)-3-(propan-2-yl)-1H-pyrazolo[3,4-b]pyridine-6-carboxylate—hydrogen chloride (1/1) HCl salt*

[00790] E197 (1.7 g, 3.42 mmol) was dissolved into 4 M HCl in dioxane (25.7 mL, 102 mmol), stirred at room temperature for two hours, and then concentrated in vacuo to give the titled compound.

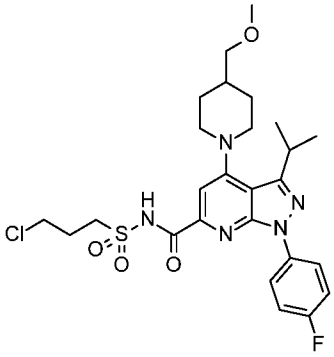
[00791] *Step 2: methyl 4-[1-(ethoxycarbonyl)piperidin-4-yl]-1-(4-fluorophenyl)-3-(propan-2-yl)-1H-pyrazolo[3,4-b]pyridine-6-carboxylate*

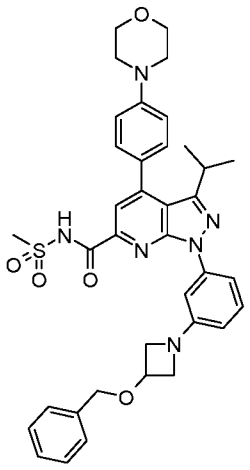
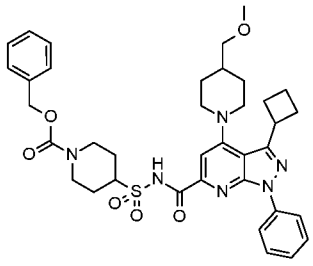
[00792] Ethyl chloroformate (67 µL, 0.7 mmol) was added dropwise at RT to a stirring solution of the compound from Step 1 (200 mg, 0.42 mmol) and DIPEA (294 µL, 1.7 mmol) in anhydrous DCM (2 mL). The reaction was complete after 2 hours. The reaction solution was diluted with DCM (10 mL) and washed with water (5 mL). The organic phase was dried over sodium sulfate, filtered and concentrated under reduced pressure to give the titled compound.

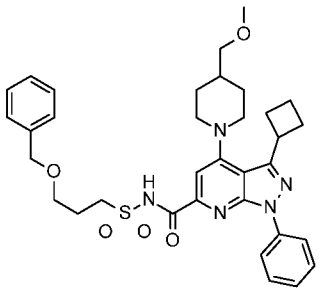
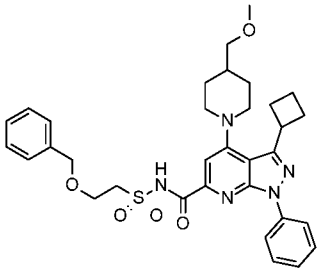
[00793] *Step 3: 4-[1-(ethoxycarbonyl)piperidin-4-yl]-1-(4-fluorophenyl)-3-(propan-2-yl)-1H-pyrazolo[3,4-b]pyridine-6-carboxylic acid*

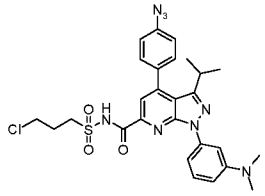
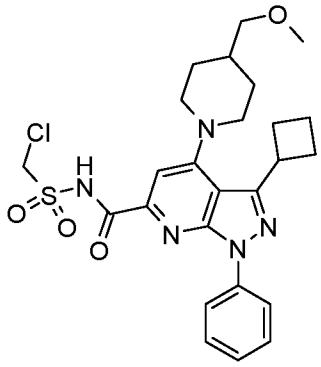
[00794] The compound from Step 2 (196 mg, 0.42 mmol) was dissolved in THF (5 mL) and aqueous 2 N sodium hydroxide (1.05 mL, 2.1 mmol) was added at RT. The solution was stirred for 20 hours. The resulting mixture was diluted with water (10 mL) and then acidified with aqueous 2 N HCl (1.05 mL). The aqueous phase was extracted twice with DCM. The combined organic phases were dried over sodium sulfate, filtered, and concentrated under reduced pressure to give the titled compound.

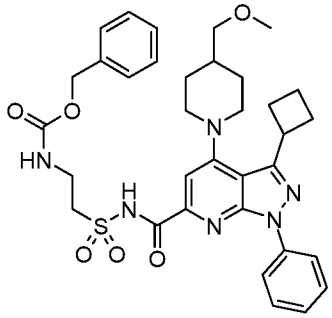
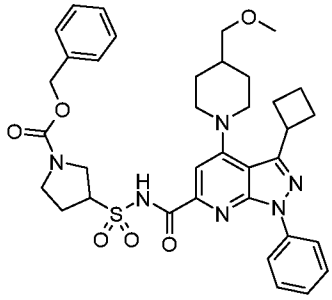
Table XVa. List of intermediate acylsulfonamides

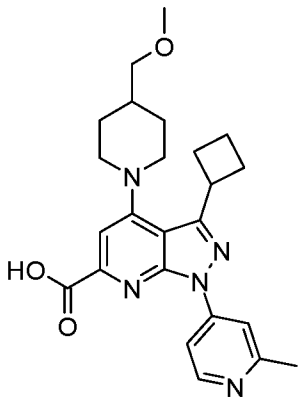
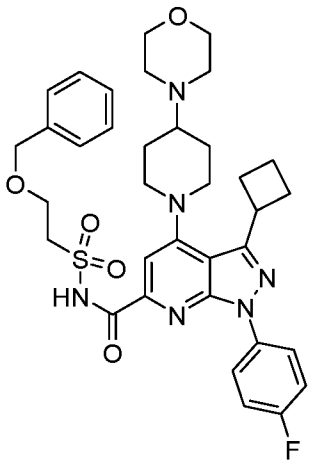
Int.	Structure	Name	SM	method	MW	Mes
AC01		*N*-(3-chloropropane-1-sulfonyl)-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	A124, 35578-28-0	Y1	566	567

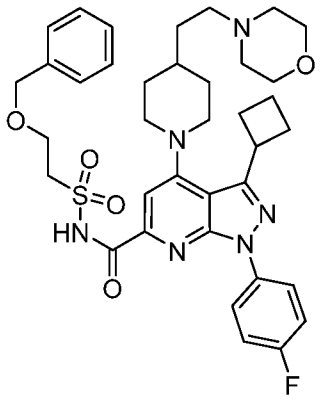
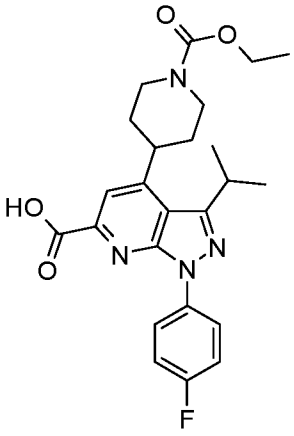
Int.	Structure	Name	SM	method	MW	Mes
AC02		1-{3-[3-(benzyloxy)azetidin-1-yl]phenyl}-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	A252, 3144-09-0	Y1	680	681
AC03		benzyl 4-({3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)piperidine-1-carboxylate	A136, S9	Y1	700	701

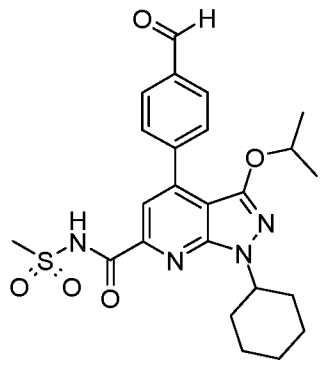
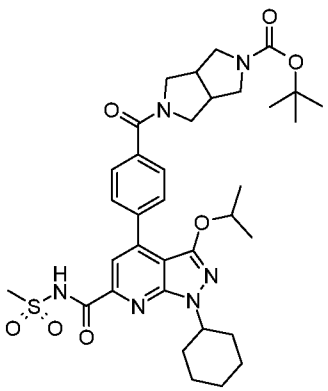
Int.	Structure	Name	SM	method	MW	Mes
AC04		*N*-[3-(benzyloxy)propane-1-sulfonyl]-3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	A136, 1408646-99-0	Y1	631	632
AC05		*N*-[2-(benzyloxy)ethanesulfonyl]-3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	A136, 881407-21-2	Y1	617	618

Int.	Structure	Name	SM	method	MW	Mes
AC06		4-(4-azidophenyl)-*N*-(3-chloropropane-1-sulfonyl)-1-[3-(dimethylamino)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	A238, 35578-28-0	Y1	580	581
AC07		*N*-(chloromethanesulfonyl)-3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	A136	Y1	532-534	533-535

Int.	Structure	Name	SM	method	MW	Mes
AC08		benzyl [2-({3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)ethyl]carbamate	A136, S5	Y1	660	661
AC09		benzyl 3-({3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)pyrrolidine-1-carboxylate	A136, S7	Y1	686	687

Int.	Structure	Name	SM	method	MW	Mes
AC10		3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-(2-methylpyridin-4-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E168	Specific example	435	436
AC11		*N*-[2-(benzyloxy)ethanesulfonyl]-3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	A308	Y1	676	677

Int.	Structure	Name	SM	method	MW	Mes
AC12		*N*-[2-(benzyloxy)ethanesulfonyl]-3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[2-(piperidin-1-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	A311	Y1	704	705
AC13		4-[1-(ethoxycarbonyl)piperidin-4-yl]-1-(4-fluorophenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxylic acid	E197	Specific example	454	455

Int.	Structure	Name	SM	method	MW	Mes
AC14		1-cyclohexyl-4-(4-formylphenyl)-*N*-(methanesulfonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	A350	Y1	484	485
AC15		*tert*-butyl 5-(4-{1-cyclohexyl-6-[(methanesulfonyl)carbamoyl]-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}benzoyl)hexahydropyrrolo[3,4-*c*]pyrrole-2(1*H*)-carboxylate	A351	Y1	694	695

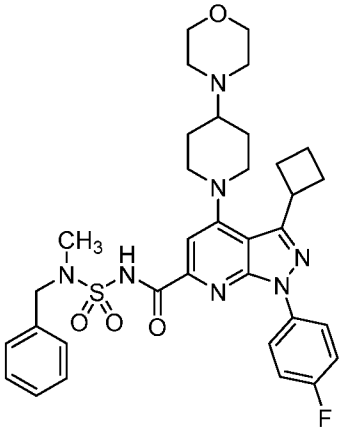
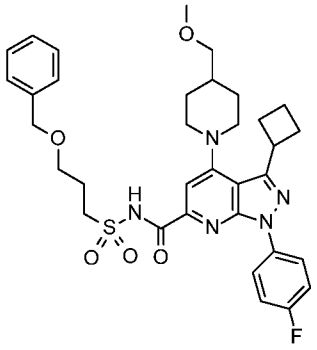
Int.	Structure	Name	SM	method	MW	Mes
AC16		*N*-[benzyl(methyl)sulfamoyl]-3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	A308, 15205-37-5	Y8	662	662
AC17		*N*-[3-(benzyloxy)propane-1-sulfonyl]-3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	A202, 1408646-99-0	Y1	649	650

Table XV. List of final compounds

Cpd Number	Name	MW	Mes	SM	Method
1	*N*-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	491	492	A002, 3144-09-0	Y1
2	*N*-(benzenesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	553	554	A002, 98-10-2	Y5
3	3-methyl-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-*N*-(trifluoromethanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	545	546	A002, 421-85-2	Y5 Specific example
4	*N*-(cyclopropanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	517	518	A002, 154350-29-5	Y1

Cpd Number	Name	MW	Mes	SM	Method
5	*N*-(ethanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	505	506	A002, 1520-70-3	Y1
6	*N*-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1-[3-(trifluoromethoxy)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	575	576	A014, 3144-09-0	Y1
7	4-[4-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-1-phenyl-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	477	478	A005, 3144-09-0	Y1
8	*N*-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	559	560	A011, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
9	1-cyclohexyl-4-[2-(dimethylamino)pyrimidin-5-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	486	487	A018, 3144-09-0	Y1
10	1-[3-(azetidin-1-yl)phenyl]-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	575	576	A038, 3144-09-0	Y1
11	1-cyclohexyl-*N*-(methanesulfonyl)-4-[2-(morpholin-4-yl)pyrimidin-5-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	527	528	A026, 3144-09-0	Y1
12	3-*tert*-butyl-1-cyclopentyl-*N*-(methanesulfonyl)-4-[6-(morpholin-4-yl)pyridin-3-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	526	527	A243, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
13	*N*-(methanesulfonyl)-3-methyl-1-phenyl-4-(piperidin-1-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	413	414	A036, 3144-09-0	Y1
14	*N*-(methanesulfonyl)-4-(4-methoxyphenyl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	436	437	A001, 3144-09-0	Y1
15	*N*-(ethanesulfonyl)-4-(4-methoxyphenyl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	451	451	A001, 1520-70-3	Y1
16	*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1-[3-(pyrrolidin-1-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	589	590	A039, 3144-09-0	Y1
17	4-[4-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-1-(6-methoxypyridin-3-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	508	509	A019, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
18	1-(3-chloro-4-methylphenyl)-*N*-(methanesulfonyl)-4-(4-methoxyphenyl)-3-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	484	485	A004, 3144-09-0	Y1
19	*N*-(ethanesulfonyl)-3-methyl-1-phenyl-4-(piperidin-1-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	428	429	A036, 1520-70-3	Y1
20	*N*-(methanesulfonyl)-4-[2-(morpholin-4-yl)pyrimidin-5-yl]-1-phenyl-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	522	523	A025, 3144-09-0	Y1
21	1-(2,4-difluorophenyl)-*N*-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	527	528	A035, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
22	1-cyclohexyl-4-[6-(dimethylamino)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	484	485	A032, 3144-09-0	Y1
23	1-(3,5-difluorophenyl)-*N*-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	527	528	A007, 3144-09-0	Y1
24	1-(3,5-dimethylphenyl)-*N*-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	519	520	A012, 3144-09-0	Y1
25	1-(3,4-difluorophenyl)-*N*-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	528	529	A015, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
26	4-[4-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-3-methyl-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	518	519	A017, 3144-09-0	Y1
27	*N*-(methanesulfonyl)-4-(4-methoxyphenyl)-3-methyl-1-(3-methylphenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	450	451	A003, 3144-09-0	Y1
28	*N*-(ethanesulfonyl)-4-(4-methoxyphenyl)-3-methyl-1-(3-methylphenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	464	465	A003, 1520-70-3	Y1
29	4-[2-(dimethylamino)pyrimidin-5-yl]-*N*-(methanesulfonyl)-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	565	566	A030, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
30	4-[2-(dimethylamino)pyrimidin-5-yl]-*N*-(ethanesulfonyl)-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	579	580	A030, 1520-70-3	Y1
31	4-[6-(dimethylamino)pyridin-3-yl]-*N*-(methanesulfonyl)-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	563	564	A031, 3144-09-0	Y1
32	4-[6-(dimethylamino)pyridin-3-yl]-*N*-(ethanesulfonyl)-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	578	579	A031, 1520-70-3	Y1

Cpd Number	Name	MW	Mes	SM	Method
33	4-[4-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	449	450	A006, 3144-09-0	Y1
34	*N*-(methanesulfonyl)-4-[6-(morpholin-4-yl)pyridin-3-yl]-1-phenyl-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	520	521	A245, 3144-09-0	Y1
35	*N*-(ethanesulfonyl)-4-[6-(morpholin-4-yl)pyridin-3-yl]-1-phenyl-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	534	535	A245, 1520-70-3	Y1
36	*N*-(methanesulfonyl)-1-[3-(3-methoxyazetidin-1-yl)phenyl]-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	604	605	A043, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
37	*N*-(methanesulfonyl)-3-methyl-4-[6-(morpholin-4-yl)pyridin-3-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	492	493	A016, 3144-09-0	Y1
38	1-(4,4-difluorocyclohexyl)-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	561	562	A040,3144-09-0	Y1
39	*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-(oxan-3-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	528	529	A020, 3144-09-0	Y1
40	*N*-(ethanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-(oxan-3-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	542	543	A020, 1520-70-3	Y1

Cpd Number	Name	MW	Mes	SM	Method
41	4-{4-[3-(dimethylamino)azetidin-1-yl]phenyl}-*N*-(methanesulfonyl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	504	505	A021, 3144-09-0	Y1
42	4-{4-[3-(dimethylamino)azetidin-1-yl]phenyl}-*N*-(ethanesulfonyl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	518	519	A021, 1520-70-3	Y1
43	1-[3-(3,3-dimethylazetidin-1-yl)phenyl]-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	603	604	A041, 3144-09-0	Y1
44	1-cyclohexyl-*N*-(methanesulfonyl)-4-[6-(morpholin-4-yl)pyridin-3-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	527	528	A247, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
45	1-cyclohexyl-*N*-(ethanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	541	542	A247, 1520-70-3	Y1
46	1-[3-(3-fluoropyrrolidin-1-yl)phenyl]-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	606	607	A044, 3144-09-0	Y1
47	1-cyclohexyl-*N*-(methanesulfonyl)-3-methyl-4-[6-(morpholin-4-yl)pyridin-3-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	499	500	A022, 3144-09-0	Y1
48	1-cyclohexyl-*N*-(ethanesulfonyl)-3-methyl-4-[6-(morpholin-4-yl)pyridin-3-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	513	514	A022, 1520-70-3	Y1

Cpd Number	Name	MW	Mes	SM	Method
49	1-cyclohexyl-4-[2-(dimethylamino)pyrimidin-5-yl]-*N*-(methanesulfonyl)-3-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	458	459	A023, 3144-09-0	Y1
50	1-cyclohexyl-4-[2-(dimethylamino)pyrimidin-5-yl]-*N*-(ethanesulfonyl)-3-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	472	473	A023, 1520-70-3	Y1
51	1-cyclohexyl-*N*-(methanesulfonyl)-4-{6-[methyl(oxan-4-yl)amino]pyridin-3-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	555	556	A045, 3144-09-0	Y1
52	methyl 3-{1-cyclohexyl-4-[2-(dimethylamino)pyrimidin-5-yl]-6-[(ethanesulfonyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-3-yl}azetidine-1-carboxylate	571	572	A249, 1520-70-3	Y1

Cpd Number	Name	MW	Mes	SM	Method
53	1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-[6-(morpholin-4-yl)pyridin-3-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	563	564	A029, 3144-09-0	Y1
54	1-[3-(dimethylamino)phenyl]-*N*-(ethanesulfonyl)-4-[6-(morpholin-4-yl)pyridin-3-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	577	578	A029, 1520-70-3	Y1
55	1-cyclopentyl-4-[6-(dimethylamino)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	471	472	A027, 3144-09-0	Y1
56	1-cyclopentyl-4-[6-(dimethylamino)pyridin-3-yl]-*N*-(ethanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	485	486	A027, 1520-70-3	Y1

Cpd Number	Name	MW	Mes	SM	Method
57	*N*-(methanesulfonyl)-3-methyl-4-[6-(morpholin-4-yl)pyridin-3-yl]-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	561	562	A033, 3144-09-0	Y1
58	*N*-(ethanesulfonyl)-3-methyl-4-[6-(morpholin-4-yl)pyridin-3-yl]-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	575	576	A033, 1520-70-3	Y1
59	1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-[2-(morpholin-4-yl)pyrimidin-5-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	564	565	A028, 3144-09-0	Y1
60	1-(2,4-difluorophenyl)-*N*-(methanesulfonyl)-3-methyl-4-[6-(morpholin-4-yl)pyridin-3-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	528	529	A034, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
61	1-(2,4-difluorophenyl)-*N*-(ethanesulfonyl)-3-methyl-4-[6-(morpholin-4-yl)pyridin-3-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	542	543	A034,1520-70-3	Y1
62	1-[3-(dimethylamino)phenyl]-*N*-(ethanesulfonyl)-4-[2-(morpholin-4-yl)pyrimidin-5-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	579	580	A028, 1520-70-3	Y1
63	3-cyclobutyl-*N*-(methanesulfonyl)-4-{6-[(2-methoxyethyl)(methyl)amino]pyridin-3-yl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	534	535	A055, 3144-09-0	Y1
64	1-cyclohexyl-4-[6-(3,3-difluoropyrrolidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	546	547	A054, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
65	1-(3-chlorophenyl)-*N*-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	525	526	A008, 3144-09-0	Y1
66	1-(3-chlorophenyl)-*N*-(ethanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	539	540	A008,1520-70-3	Y1
67	1-(3-fluorophenyl)-*N*-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	509	510	A009, 3144-09-0	Y1
68	*N*-(ethanesulfonyl)-1-(3-fluorophenyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	523	524	A009, 1520-70-3	Y1

Cpd Number	Name	MW	Mes	SM	Method
69	*N*-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1-[4-(trifluoromethoxy)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	575	576	A013, 3144-09-0	Y1
70	*N*-(ethanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1-[4-(trifluoromethoxy)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	589	590	A013, 1520-70-3	Y1
71	4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	555	556	A056, 3144-09-0	Y1 Specific example
72	*N*-(methanesulfonyl)-1-(3-methoxyphenyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	521	522	A010, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
73	*N*-(ethanesulfonyl)-1-(3-methoxyphenyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	535	536	A010, 1520-70-3	Y1
74	3-cyclobutyl-*N*-(methanesulfonyl)-4-{6-[methyl(oxan-4-yl)amino]pyridin-3-yl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	560	561	A057, 3144-09-0	Y1
75	3-cyclobutyl-*N*-(methanesulfonyl)-4-{4-[(2-methoxyethyl)(methyl)amino]phenyl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	533	534	A058, 3144-09-0	Y1
76	*N*-(methanesulfonyl)-1-{3-[(2-methoxyethyl)(methyl)amino]phenyl}-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	607	608	A047, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
77	1-[3-(dimethylamino)phenyl]-4-[2-(dimethylamino)pyrimidin-5-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	522	523	A024, 3144-09-0	Y1
78	1-[3-(dimethylamino)phenyl]-4-[2-(dimethylamino)pyrimidin-5-yl]-*N*-(ethanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	537	538	A024, 1520-70-3	Y1
79	4-(4-acetamidophenyl)-1-cyclohexyl-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	497	498	A046, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
80	4-[4-(4-cyanopiperidin-1-yl)phenyl]-1-cyclohexyl-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	548	549	A059, 3144-09-0	Y1
81	4-[4-(4-cyanopiperidin-1-yl)phenyl]-1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	585	586	A048, 3144-09-0	Y1
82	1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-{4-[(2-methoxyethyl)(methyl)amino]phenyl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	564	565	A049, 3144-09-0	Y1
83	4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	586	587	A050, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
84	1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-{6-[(2-methoxyethyl)(methyl)amino]pyridin-3-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	565	566	A051, 3144-09-0	Y1
85	4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	628	629	A052, 3144-09-0	Y1
86	*N*-(methanesulfonyl)-4-{6-[(2-methoxyethyl)(methyl)amino]pyridin-3-yl}-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	608	609	A053, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
87	*N*-(methanesulfonyl)-4-{6-[methyl(oxan-4-yl)amino]pyridin-3-yl}-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	634	635	A060, 3144-09-0	Y1
88	*N*-(methanesulfonyl)-4-{4-[(2-methoxyethyl)(methyl)amino]phenyl}-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	607	608	A061, 3144-09-0	Y1
89	1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-{6-[methyl(oxan-4-yl)amino]pyridin-3-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	591	592	A062, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
90	1-cyclohexyl-*N*-(ethanesulfonyl)-4-{6-[methyl(oxan-4-yl)amino]pyridin-3-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	568	569	A045, 1520-70-3	Y1
91	1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-{2-[methyl(oxan-4-yl)amino]pyrimidin-5-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	593	594	A068, 3144-09-0	Y1
92	1-cyclohexyl-3-cyclopropyl-4-[6-(dimethylamino)pyridin-3-yl]-*N*-(ethanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	497	498	A251, 1520-70-3	Y1
93	1-cyclohexyl-4-[6-(2,6-dimethylmorpholin-4-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	554	555	A065, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
94	1-cyclohexyl-4-[6-(2,2-dimethylmorpholin-4-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	554	555	A066, 3144-09-0	Y1
95	4-[2-(4-cyanopiperidin-1-yl)pyrimidin-5-yl]-1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	588	589	A067, 3144-09-0	Y1
96	1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-{4-[methyl(oxan-4-yl)amino]phenyl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	590	591	A072, 3144-09-0	Y1
97	*N*-(methanesulfonyl)-4-{4-[methyl(oxan-4-yl)amino]phenyl}-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	632	633	A073, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
98	4-[6-(4-cyano-4-methylpiperidin-1-yl)pyridin-3-yl]-1-cyclohexyl-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	563	564	A070, 3144-09-0	Y1
99	4-[2-(4-cyanopiperidin-1-yl)pyrimidin-5-yl]-*N*-(methanesulfonyl)-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	629	630	A071, 3144-09-0	Y1
100	4-{4-[3-(dimethylamino)pyrrolidin-1-yl]phenyl}-*N*-(methanesulfonyl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	519	520	A075, 3144-09-0	Y1
101	*N*-(methanesulfonyl)-1-(3-methylphenyl)-4-(piperidin-1-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	456	457	A042, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
102	*N*-(ethanesulfonyl)-1-(3-methylphenyl)-4-(piperidin-1-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	470	471	A042, 1520-70-3	Y1
103	4-[4-(4-cyanopiperidin-1-yl)phenyl]-3-cyclobutyl-1-cyclohexyl-*N*-(methanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	561	562	A076, 3144-09-0	Y1
104	4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-cyclobutyl-1-cyclohexyl-*N*-(methanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	562	563	A077, 3144-09-0	Y1
105	1-[3-(3-hydroxyazetidin-1-yl)phenyl]-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	591	592	AC02	Y6 Specific example

Cpd Number	Name	MW	Mes	SM	Method
106	1-cyclohexyl-*N*-(methanesulfonyl)-4-[6-(3-methoxypyrrolidin-1-yl)pyridin-3-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	540	541	A080, 3144-09-0	Y1
107	methyl 3-{4-(4-acetamidophenyl)-1-(3,5-difluorophenyl)-6-[(methanesulfonyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-3-yl}azetidine-1-carboxylate	598	599	A078, 3144-09-0	Y1
108	1-cyclohexyl-4-[6-(3-fluoropiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	542	543	A079, 3144-09-0	Y1
109	*N*-(methanesulfonyl)-4-{4-[(2-methoxyethyl)(methyl)amino]phenyl}-3-(propan-2-yl)-1-[3-(pyrrolidin-1-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	590	591	A087, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
110	*N*-(methanesulfonyl)-4-{4-[methyl(oxan-4-yl)amino]phenyl}-3-(propan-2-yl)-1-[3-(pyrrolidin-1-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	617	618	A090, 3144-09-0	Y1
111	3-cyclobutyl-*N*-(methanesulfonyl)-4-{4-[methyl(oxan-4-yl)amino]phenyl}-1-[3-(pyrrolidin-1-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	628	629	A091, 3144-09-0	Y1
112	*N*-(ethanesulfonyl)-4-[2-(morpholin-4-yl)pyrimidin-5-yl]-1-phenyl-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	536	537	A025, 1520-70-3	Y1
113	1-(2,4-difluorophenyl)-*N*-(ethanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	542	543	A035, 1520-70-3	Y1

Cpd Number	Name	MW	Mes	SM	Method
114	1-(3-chloro-4-methylphenyl)-*N*-(ethanesulfonyl)-4-(4-methoxyphenyl)-3-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	498	499	A004, 1520-70-3	Y1
115	1-(3,5-dimethylphenyl)-*N*-(ethanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	534	535	A012, 1520-70-3	Y1
116	1-(3,4-difluorophenyl)-*N*-(ethanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	542	543	A015, 1520-70-3	Y1
117	*N*-(methanesulfonyl)-4-(4-methoxypiperidin-1-yl)-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	486	487	A064, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
118	*N*-(ethanesulfonyl)-4-(4-methoxypiperidin-1-yl)-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	500	501	A064, 1520-70-3	Y1
119	4-[2-(4-cyanopiperidin-1-yl)pyrimidin-5-yl]-1-cyclohexyl-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	551	552	A084, 3144-09-0	Y1
120	1-cyclohexyl-*N*-(methanesulfonyl)-4-{2-[(2-methoxyethyl)(methyl)amino]pyrimidin-5-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	530	531	A086, 3144-09-0	Y1
121	4-{6-[bis(2-methoxyethyl)amino]pyridin-3-yl}-1-cyclohexyl-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	572	573	A100, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
122	1-cyclohexyl-*N*-(methanesulfonyl)-4-{6-[methyl(oxolan-3-yl)amino]pyridin-3-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	540	541	A101, 3144-09-0	Y1
123	1-cyclohexyl-*N*-(methanesulfonyl)-4-{2-[methyl(oxan-4-yl)amino]pyrimidin-5-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	556	557	A085, 3144-09-0	Y1
124	4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	612	613	A093, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
125	1-[6-(dimethylamino)pyridin-2-yl]-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	563	564	A097, 3144-09-0	Y1
126	*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1-[3-(trifluoromethoxy)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	603	604	A098, 3144-09-0	Y1
127	1-(3,4-difluorophenyl)-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	555	556	A088, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
128	*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-[6-(morpholin-4-yl)pyridin-2-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	605	606	A089, 3144-09-0	Y1
129	4-(2,6-difluoro-4-methoxyphenyl)-1-(3-fluoro-5-methoxyphenyl)-*N*-(methanesulfonyl)-3-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	520	521	A103, 3144-09-0	Y1
130	4-[4-(4-cyanopiperidin-1-yl)phenyl]-1-(3,5-difluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	579	580	A104, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
131	4-[4-(4-cyanopiperidin-1-yl)phenyl]-1-(3-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	561	562	A105, 3144-09-0	Y1
132	*N*-(methanesulfonyl)-4-{4-[(2-methoxyethyl)(methyl)amino]phenyl}-3-(propan-2-yl)-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	590	591	A106, 3144-09-0	Y1
133	*N*-(methanesulfonyl)-4-{6-[methyl(oxan-4-yl)amino]pyridin-3-yl}-3-(propan-2-yl)-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	617	618	A107, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
134	1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-{2-[methyl(oxan-4-yl)amino]pyrimidin-5-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	567	568	A102, 3144-09-0	Y1
135	4-[4-(4-cyanopiperidin-1-yl)phenyl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	611	612	A094, 3144-09-0	Y1
136	*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-[2-(morpholin-4-yl)pyridin-4-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	605	606	A069, 3144-09-0	Y1
137	*N*-(methanesulfonyl)-3-(1-methylcyclobutyl)-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	546	547	A114, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
138	*N*-(ethanesulfonyl)-3-(1-methylcyclobutyl)-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	560	561	A114, 1520-70-3	Y1
139	4-[2-(4-cyanopiperidin-1-yl)pyrimidin-5-yl]-1-(2,4-difluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	581	582	A108, 3144-09-0	Y1
140	4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-1-(2,4-difluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	580	581	A109, 3144-09-0	Y1
141	4-[4-(4-cyanopiperidin-1-yl)phenyl]-1-(2,4-difluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	579	580	A110, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
142	3-cyclobutyl-*N*-(methanesulfonyl)-4-(4-methoxypiperidin-1-yl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	483	484	A116, 3144-09-0	Y1
143	3-cyclobutyl-*N*-(1,1-dioxo-1λ^6-thiolane-3-sulfonyl)-4-(4-methoxypiperidin-1-yl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	588	589	A116, 17115-48-9	Y1
144	1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	528	529	A119, 3144-09-0	Y1
145	4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-1-(oxan-3-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	552	553	A117, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
146	3-cyclobutyl-*N*-(2-methoxyethanesulfonyl)-4-(4-methoxypiperidin-1-yl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	527	528	A116, 51517-04-5	Y1
147	3-cyclobutyl-4-(4-methoxypiperidin-1-yl)-1-phenyl-*N*-(3,3,3-trifluoropropane-1-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	566	567	A116, 1033906-44-3	Y1
148	3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	531	532	A037, 3144-09-0	Y1
149	4-(1,1-difluoro-5-azaspiro[2.4]heptan-5-yl)-*N*-(methanesulfonyl)-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	504	505	A099, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
150	1-cyclohexyl-*N*-(methanesulfonyl)-4-(4-methoxypiperidin-1-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	478	479	A096, 3144-09-0	Y1
151	3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-4-{4-[(propan-2-yl)oxy]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	512	513	A121, 3144-09-0	Y1
152	3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-4-(4-propoxypiperidin-1-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	511	512	A210, 3144-09-0	Y1
153	3-cyclobutyl-*N*-(methanesulfonyl)-4-[3-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	497	498	A122, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
154	3-cyclobutyl-*N*-(methanesulfonyl)-4-{4-[2-oxo-2-(pyrrolidin-1-yl)ethoxy]piperidin-1-yl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	581	582	A118, 3144-09-0	Y1
155	1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-(4-methoxypiperidin-1-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	514	515	A113, 3144-09-0	Y1
156	*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	500	501	A082, 3144-09-0	Y1
157	1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-(piperidin-1-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	484	485	A111, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
158	4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1-[2-(pyrrolidin-1-yl)pyridin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	614	615	A120, 3144-09-0	Y1
159	3-cyclobutyl-*N*-(methanesulfonyl)-4-(1-oxa-7-azaspiro[3.5]nonan-7-yl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	496	497	A211, 3144-09-0	Y1
160	4-(4-cyanopiperidin-1-yl)-1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	510	511	A112, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
161	*N*-(methanesulfonyl)-4-[4-(2-methoxyethyl)piperidin-1-yl]-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	514	515	A083, 3144-09-0	Y1
162	*N*-(methanesulfonyl)-4-(3-methoxypiperidin-1-yl)-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	486	487	A063, 3144-09-0	Y1
163	*N*-(ethanesulfonyl)-4-(3-methoxypiperidin-1-yl)-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	500	501	A063, 1520-70-3	Y1
164	4-[4-(fluoromethyl)piperidin-1-yl]-*N*-(methanesulfonyl)-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	487	488	A115, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
165	*N*-(methanesulfonyl)-4-[4-(methanesulfonyl)piperidin-1-yl]-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	533	534	A092, 3144-09-0	Y1
166	*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	536		A123, 3144-09-0	Y1
167	1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(4-methoxypiperidin-1-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	489	490	A126, 3144-09-0	Y1
168	1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	503	504	A124, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
169	4-[4-(4-cyanopiperidin-1-yl)phenyl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1-[2-(pyrrolidin-1-yl)pyridin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	613	614	A125, 3144-09-0	Y1
170	*N*-(methanesulfonyl)-4-[(2-methoxyethyl)(methyl)amino]-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	460	461	A074, 3144-09-0	Y1
171	*N*-(methanesulfonyl)-1-(3-methylphenyl)-4-(8-oxa-2-azaspiro[4.5]decan-2-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	511	512	A095, 3144-09-0	Y1
172	4-(4-butoxypiperidin-1-yl)-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	532	533	A127, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
173	1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(4-methoxy-4-methylpiperidin-1-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	504	505	A129, 3144-09-0	Y1
174	2-[(2-{[3-cyclobutyl-4-(4-methoxypiperidin-1-yl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl]sulfamoyl}ethyl)carbamoyl]benzoic acid	661	662	A116,	Y1
175	1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[4-(2-methylpropoxy)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	531	532	A128, 3144-09-0	Y1
176	3-cyclobutyl-4-(4-methoxypiperidin-1-yl)-1-phenyl-*N*-(2,2,2-trifluoroethanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	551	552	A116, 67497-95-4	Y1

Cpd Number	Name	MW	Mes	SM	Method
177	1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(1-oxa-7-azaspiro[3.5]nonan-7-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	502	503	A130, 3144-09-0	Y1
178	4-[3-(difluoromethyl)piperidin-1-yl]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	510	511	A131, 3144-09-0	Y1
179	1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(6-oxa-2-azaspiro[3.5]nonan-2-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	502	503	A132, 3144-09-0	Y1
180	1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(1-oxa-8-azaspiro[4.5]decan-8-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	515	516	A133, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
181	3-cyclobutyl-4-(cyclohexylmethoxy)-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	482	483	A138, 3144-09-0	Y1
182	3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-4-(piperidin-1-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	453	454	A139, 3144-09-0	Y1
183	3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(2-methoxyethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	512	513	A134, 3144-09-0	Y1
184	4-(2-azaspiro[3.4]octan-2-yl)-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	480	481	A135, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
185	3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	497	498	A136, 3144-09-0	Y1
186	4-(3-azabicyclo[3.1.0]hexan-3-yl)-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	452	453	A137, 3144-09-0	Y1
187	*N*-(methanesulfonyl)-4-(4-methoxypiperidin-1-yl)-1-[2-(morpholin-4-yl)pyridin-4-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	557	558	A212, 3144-09-0	Y1
188	*N*-(methanesulfonyl)-4-(4-methoxypiperidin-1-yl)-3-(propan-2-yl)-1-[2-(pyrrolidin-1-yl)pyridin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	541	542	A143, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
189	4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-cyclobutyl-*N*-(methanesulfonyl)-1-[2-(pyrrolidin-1-yl)pyridin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	626	627	A144, 3144-09-0	Y1
190	3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(methanesulfonyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	531	532	A142, 3144-09-0	Y1
191	4-(4-cyanopiperidin-1-yl)-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	478	479	A141, 3144-09-0	Y1
192	4-(2-azaspiro[3.5]nonan-2-yl)-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	493	494	A140, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
193	3-cyclobutyl-*N*-(methanesulfonyl)-4-[3-(methoxymethyl)azetidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	469	470	A149, 3144-09-0	Y1
194	4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(*cis*-3-methoxycyclobutyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	586	587	A152, 3144-09-0	Y1
195	4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-(3,3-difluorocyclobutyl)-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	592	593	A151, 3144-09-0	Y1
196	4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-(3,3-dimethylcyclobutyl)-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	584	585	A161, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
197	4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-(3-fluorocyclobutyl)-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	574	575	A258, 3144-09-0	Y1
198	3-cyclobutyl-*N*-(methanesulfonyl)-4-[2-(oxan-4-yl)ethoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	499	500	A145, 3144-09-0	Y1
199	3-cyclobutyl-4-[(2*S*)-2-fluoro-2-(oxan-4-yl)ethoxy]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	516	517	A146, 3144-09-0	Y1
200	3-cyclobutyl-*N*-(methanesulfonyl)-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	485	486	A148, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
201	4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-cyclobutyl-*N*-(methanesulfonyl)-1-[2-(morpholin-4-yl)pyridin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	641	642	A147, 3144-09-0	Y1
202	3-cyclobutyl-4-(1,1-difluoro-5-azaspiro[2.4]heptan-5-yl)-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	502	503	A154, 3144-09-0	Y1
203	3-cyclobutyl-*N*-(methanesulfonyl)-4-(5-oxa-2-azaspiro[3.5]nonan-2-yl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	496	497	A155, 3144-09-0	Y1
204	3-cyclobutyl-*N*-(methanesulfonyl)-4-(7-oxa-2-azaspiro[3.5]nonan-2-yl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	496	497	A156, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
205	4-(5-azaspiro[2.5]octan-5-yl)-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	480	481	A150, 3144-09-0	Y1
206	3-cyclobutyl-*N*-(methanesulfonyl)-4-[(2-methoxyethyl)(methyl)amino]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	458	459	A153, 3144-09-0	Y1
207	3-cyclobutyl-4-(4-methoxypiperidin-1-yl)-*N*-(oxane-4-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	553	554	A116, S8	Y1
208	benzyl 4-{[3-cyclobutyl-4-(4-methoxypiperidin-1-yl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl]sulfamoyl}piperidine-1-carboxylate	686	687	A116, S9	Y1

Cpd Number	Name	MW	Mes	SM	Method
209	4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-(*cis*-3-fluorocyclobutyl)-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	574	575	197	Preparative HPLC
210	4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-(*trans*-3-fluorocyclobutyl)-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	574	575	197	Preparative HPLC
211	3-cyclobutyl-*N*-(methanesulfonyl)-4-[(*cis*-4-methoxycyclohexyl)oxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	498	499	A159, 3144-09-0	Y1
212	3-cyclobutyl-*N*-(methanesulfonyl)-4-[(*trans*-4-methoxycyclohexyl)oxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	499	500	A160, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
213	4-{4-[(benzyloxy)methyl]piperidin-1-yl}-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	574	575	A158, 3144-09-0	Y1
214	4-(2-azaspiro[3.3]heptan-2-yl)-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	466	467	A157, 3144-09-0	Y1
215	methyl 5-{3-cyclobutyl-6-[(methanesulfonyl)carbamoyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}octahydro-1*H*-pyrrolo[3,2-*c*]pyridine-1-carboxylate	552	553	A213, 3144-09-0	Y1
216	4-(1-acetyloctahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl)-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	537	538	A214, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
217	*N*-(methanesulfonyl)-4-(4-methoxypiperidin-1-yl)-1-[6-(morpholin-4-yl)pyridin-2-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	558	559	A215, 3144-09-0	Y1
218	1-cyclohexyl-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	491	492	A162, 3144-09-0	Y1
219	3-cyclobutyl-4-{4-[(1*S*)-2-(dimethylamino)-1-fluoroethyl]piperidin-1-yl}-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	543	544	A170, 3144-09-0	Y1
220	3-cyclobutyl-4-[4-(fluoromethyl)piperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	486	487	A216, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
221	1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[4-(2-methoxypropan-2-yl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	531	532	A169, 3144-09-0	Y1
222	4-(3-azaspiro[5.5]undecan-3-yl)-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	521	522	A217, 3144-09-0	Y1
223	1-(3,4-difluorophenyl)-*N*-(ethanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	569	570	A088, 1520-70-3	Y1
224	*N*-(ethanesulfonyl)-1-(3-fluorophenyl)-4-{6-[methyl(oxan-4-yl)amino]pyridin-3-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	580	581	A255, 1520-70-3	Y1

Cpd Number	Name	MW	Mes	SM	Method
225	*N*-(cyclopropanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	561	562	A123, 154350-29-5	Y1
226	*N*-(2-methoxyethanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	579	580	A123, 51517-04-5	Y1
227	4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-1-[2-(morpholin-4-yl)pyridin-4-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	630	631	A168, 3144-09-0	Y1
228	3-cyclobutyl-4-[4-(cyclopentyloxy)piperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	537	538	A218, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
229	3-cyclobutyl-4-[4-(cyclohexyloxy)piperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	551	552	A219, 3144-09-0	Y1
230	3-cyclobutyl-4-[4-(cyclopropylmethoxy)piperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	524	525	A220, 3144-09-0	Y1
231	*N*-(2-methoxyethanesulfonyl)-4-(4-methoxyphenyl)-3-methyl-1-(2-methylpropyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	460	461	A221, 51517-04-5	Y1
232	*N*-(2-methoxyethanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-(oxolan-3-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	557	558	A254, 51517-04-5	Y1

Cpd Number	Name	MW	Mes	SM	Method
233	*N*-(2-methoxyethanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	521	522	A222, 51517-04-5	Y1
234	*N*-(2-methoxyethanesulfonyl)-4-(4-methoxyphenyl)-3-methyl-1-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	446	447	A223, 51517-04-5	Y1
235	1-cyclopropyl-*N*-(2-methoxyethanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	499	500	A224, 51517-04-5	Y1
236	1-(4-fluorophenyl)-*N*-(2-methoxyethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	547	548	A124, 51517-04-5	Y1

Cpd Number	Name	MW	Mes	SM	Method
237	3-cyclobutyl-4-[(2*R*)-2-fluoro-2-(oxan-4-yl)ethoxy]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	516	517	A165, 3144-09-0	Y1
238	3-cyclobutyl-4-[(3,3-difluorocyclopentyl)methoxy]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	505	506	A166, 3144-09-0	Y1
239	1-cyclohexyl-*N*-(cyclopropanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	523	524	A226, 154350-29-5	Y1
240	4-(4-cyanopiperidin-1-yl)-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	484	485	A227, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
241	3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(1-methoxyethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	511	512	A175, 3144-09-0	Y1
242	3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-4-[4-(1,1,1-trifluoro-2-methoxypropan-2-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	580	581	A176, 3144-09-0	Y1
243	3-cyclobutyl-4-[2-(1,1-dioxo-1λ^6,4-thiazinan-4-yl)ethoxy]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	548	549	A167, 3144-09-0	Y1
244	3-cyclobutyl-4-[4-(hydroxymethyl)piperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	484	485	A413 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
245	3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-(1-methyl-1*H*-pyrazole-4-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	564	565	A136, 288148-34-5	Y4
246	4-{6-[bis(2-methoxyethyl)amino]pyridin-3-yl}-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	579	580	A177, 3144-09-0	Y1
247	3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-methoxy-4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	527	528	A180, 3144-09-0	Y1
248	*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-[2-(morpholin-4-yl)pyridin-4-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	571	572	A179, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
249	*N*-(2-methoxyethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-[2-(morpholin-4-yl)pyridin-4-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	615	616	A179, 51517-04-5	Y1
250	3-cyclobutyl-*N*-(1,2-dimethyl-1*H*-imidazole-4-sulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	578	579	A136, 137049-02-6	Y1
251	1-cyclohexyl-*N*-(2-methoxyethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	535	536	A162, 51517-04-5	Y1

Cpd Number	Name	MW	Mes	SM	Method
252	4-{6-[bis(2-methoxyethyl)amino]pyridin-3-yl}-*N*-(methanesulfonyl)-1-[2-(morpholin-4-yl)pyridin-4-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	653	654	A178, 3144-09-0	Y1
253	3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-*N*-(1*H*-pyrazole-4-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	549	550	A136, 438630-64-9	Y4
254	3-cyclobutyl-*N*-(methanesulfonyl)-4-[(3-methyloxetan-3-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	470	471	A174, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
255	3-cyclobutyl-4-{4-[(1,1-dioxo-1λ^6,4-thiazinan-4-yl)methyl]-4-methoxypiperidin-1-yl}-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	630	631	A253, 3144-09-0	Y1
256	3-cyclobutyl-*N*-(2-methoxyethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	541	542	A136, 51517-04-5	Y1 Specific example
257	4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(*trans*-3-methylcyclobutyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	569	570	A183, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
258	4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-1-phenyl-3-[(piperidin-4-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	600	601	259	Y6 Specific example
259	*tert*-butyl 4-({4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-6-[(methanesulfonyl)carbamoyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-3-yl}oxy)piperidine-1-carboxylate	700	701	A184, 3144-09-0	Y1
260	3-cyclobutyl-*N*-[2-(1,3-dioxo-1,3-dihydro-2*H*-isoindol-2-yl)ethanesulfonyl]-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	656	657	A136,4443-23-6	Y1

Cpd Number	Name	MW	Mes	SM	Method
261	*N*-(2-aminoethanesulfonyl)-3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	526	527	260	Y6 Specific example
262	1-(cyclobutylmethyl)-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	477	478	A181, 3144-09-0	Y1
263	1-(cyclobutylmethyl)-*N*-(2-methoxyethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	521	522	A181, 51517-04-5	Y1

Cpd Number	Name	MW	Mes	SM	Method
264	*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-(2-methylpropyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	465	466	A182, 3144-09-0	Y1
265	*N*-(2-methoxyethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-(2-methylpropyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	509	510	A182, 51517-04-5	Y1
266	1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-4-[4-(2,2,2-trifluoroethyl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	542	543	A241, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
267	3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[2-(morpholin-4-yl)ethanesulfonyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	597	598	A136, S1	Y1
268	*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-(1-methyl-6-oxo-1,6-dihydropyridazin-3-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	517	518	A228, 3144-09-0	Y1
269	3-cyclobutyl-*N*-(2-methoxyethanesulfonyl)-4-[(3-methyloxetan-3-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	515	516	A174, 51517-04-5	Y1
270	3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-4-[4-(propan-2-yl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	497	498	A239, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
271	3-cyclobutyl-*N*-(2-methoxyethanesulfonyl)-1-phenyl-4-[4-(propan-2-yl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	541	542	A239, 51517-04-5	Y1
272	1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[3-(morpholin-4-yl)propane-1-sulfonyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	617	618	A124, S10	Y1
273	3-cyclobutyl-*N*-[2-(dimethylamino)ethanesulfonyl]-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	555	556	A136, 71365-70-3	Y1
274	4-[(1-acetyl-4-fluoropiperidin-4-yl)methoxy]-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	543	544	A172, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
275	4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(2-methoxyethanesulfonyl)-3-[(oxolan-3-yl)oxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	632	633	A186, 51517-04-5	Y1
276	4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(2-methoxyethanesulfonyl)-3-(*trans*-3-methylcyclobutyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	614	615	A183, 51517-04-5	Y1
277	4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-[(oxolan-3-yl)oxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	587	588	A186, 3144-09-0	Y1
278	1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-[(oxan-4-yl)methoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	515	516	A188, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
279	*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-[2-(morpholin-4-yl)pyrimidin-4-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	572	573	A185, 3144-09-0	Y1
280	4-(4-cyclobutylpiperazin-1-yl)-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	514	515	A240, 3144-09-0	Y1
281	3-cyclobutyl-*N*-(methanesulfonyl)-4-[3-(morpholin-4-yl)propoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	513	514	A173, 3144-09-0	Y1
282	3-cyclobutyl-4-[(3,3-difluoro-1-methylcyclobutyl)methoxy]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	505	506	A171, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
283	3-cyclobutyl-*N*-(methanesulfonyl)-4-[(oxolan-2-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	470	471	A260	Y1
284	1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[(oxan-4-yl)methoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	490	491	A189, 3144-09-0	Y1
285	1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[2-(oxan-4-yl)ethoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	504	505	A190, 3144-09-0	Y1
286	3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-(1-methyl-1*H*-imidazole-4-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	564	565	A136, 137049-00-4	Y4

Cpd Number	Name	MW	Mes	SM	Method
287	3-cyclobutyl-*N*-(3,5-dimethyl-1,2-oxazole-4-sulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	579	580	A136, 80466-79-1	Y4 Specific example
288	methyl 3-({3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)propanoate	570	571	A136, S2	Y1
289	3-({3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)propanoic acid	556	557	288	Y2 Specific example

Cpd Number	Name	MW	Mes	SM	Method
290	*N*-[3-(dimethylamino)propane-1-sulfonyl]-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	574	575	AC01, 124-40-3	Y3 Specific example
291	1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-*N*-[3-(pyrrolidin-1-yl)propane-1-sulfonyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	601	602	AC01	Y3
292	1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[3-(morpholin-4-yl)propoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	519	520	A193, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
293	1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[(3-methyloxetan-3-yl)methoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	476	477	A194, 3144-09-0	Y1
294	3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(2-methoxypropan-2-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	526	527	A191, 3144-09-0	Y1
295	1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[(oxolan-2-yl)methoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	476	477	A195, 3144-09-0	Y1
296	4-[(1-acetylpiperidin-4-yl)methoxy]-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	525	526	A225, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
297	methyl 4-[({3-cyclobutyl-6-[(methanesulfonyl)carbamoyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}oxy)methyl]piperidine-1-carboxylate	542	543	A237, 3144-09-0	Y1
298	3-cyclobutyl-*N*-[3-(dimethylamino)-3-oxopropane-1-sulfonyl]-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	583	584	289, 124-40-3	Y2 Specific example
299	4-[3-(dimethylamino)propoxy]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	477	478	A192, 3144-09-0	Y1
300	4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-[(oxetan-3-yl)oxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	573	574	A187, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
301	1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[(2-methoxyethyl)(methyl)amino]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	463	464	A229, 3144-09-0	Y1
302	*N*-[3-(azetidin-1-yl)propane-1-sulfonyl]-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	587	588	AC01	Y3
303	3-cyclobutyl-4-[3-(dimethylamino)propoxy]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	472	473	A196, 3144-09-0	Y1
304	1-(4-fluorophenyl)-4-[4-(2-hydroxypropan-2-yl)piperidin-1-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	518	519	A201, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
305	1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[2-(1-methylpiperidin-2-yl)ethoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	518	519	A230, 3144-09-0	Y1
306	4-[(3,3-difluoro-1-methylcyclobutyl)methoxy]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	510	511	A198, 3144-09-0	Y1
307	1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[3-(piperidin-1-yl)propoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	517	518	A199, 3144-09-0	Y1
308	4-[(1-acetyl-4-fluoropiperidin-4-yl)methoxy]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	549	550	A231, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
309	1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-{2-[(oxetan-3-yl)(propan-2-yl)amino]ethoxy}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	533	534	A232, 3144-09-0	Y1
310	1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-4-{[4-(propan-2-yl)morpholin-3-yl]methoxy}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	533	534	A233, 3144-09-0	Y1
311	4-[(1,3-dimethoxypropan-2-yl)oxy]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	494	495	A200, 3144-09-0	Y1
312	4-[(1,4-dioxan-2-yl)methoxy]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	492	493	A234, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
313	1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-{2-[(oxetan-3-yl)oxy]ethoxy}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	492	493	A235, 3144-09-0	Y1
314	3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-4-[3-(piperidin-1-yl)propoxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	512	513	A197, 3144-09-0	Y1
315	3-cyclobutyl-*N*-(2-methoxyethanesulfonyl)-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	528	529	A148, 51517-04-5	Y1
316	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	515	516	A202, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
317	3-cyclobutyl-4-[4-(2-hydroxypropan-2-yl)piperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	512	513	A204, 3144-09-0	Y1
318	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[(oxan-4-yl)methoxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	503	504	A203, 3144-09-0	Y1
319	4-[4-(dimethylamino)piperidin-1-yl]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	502	503	A205, 3144-09-0	Y1
320	1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(1'-methyl[4,4'-*b*ipiperidin]-1-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	556	557	A206, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
321	4-[(1-acetylpiperidin-4-yl)methoxy]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	531	532	A207, 3144-09-0	Y1
322	methyl 4-({[1-(4-fluorophenyl)-6-[(methanesulfonyl)carbamoyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl]oxy}methyl)piperidine-1-carboxylate	547	548	A208, 3144-09-0	Y1
323	3-cyclobutyl-*N*-(methanesulfonyl)-4-[2-(1-methylpiperidin-2-yl)ethoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	511	512	A264, 3144-09-0	Y1
324	3-cyclobutyl-4-[(1,3-dimethoxypropan-2-yl)oxy]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	488	489	A265, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
325	3-cyclobutyl-*N*-(methanesulfonyl)-4-{2-[(oxetan-3-yl)(propan-2-yl)amino]ethoxy}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	527	528	A266, 3144-09-0	Y1
326	4-[4-(cyanomethyl)-4-hydroxypiperidin-1-yl]-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	508	509	A267	Y1
327	4-(4-azidophenyl)-*N*-(3-azidopropane-1-sulfonyl)-1-[3-(dimethylamino)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	587	588	AC06	Y7 Specific example
328	3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	538	538	A268, 3144-09-0	Y1 Specific example

Cpd Number	Name	MW	Mes	SM	Method
329	3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-4-[4-(2,2,2-trifluoroethyl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	536	537	A269, 3144-09-0	Y1
330	3-cyclobutyl-*N*-(2-methoxyethanesulfonyl)-1-phenyl-4-[4-(2,2,2-trifluoroethyl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	580	581	A269, 51517-04-5	Y1
331	3-cyclobutyl-*N*-(methanesulfonyl)-4-{4-[2-(morpholin-4-yl)ethyl]piperidin-1-yl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	566	567	A270,3144-09-0	Y1 Specific example
332	4-[(3a*R*,7a*S*)-1-acetyloctahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl]-3-cyclobutyl-*N*-[3-(morpholin-4-yl)propane-1-sulfonyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	649	650	A271, S10	Y1 Specific example

Cpd Number	Name	MW	Mes	SM	Method
333	3-cyclobutyl-*N*-(cyclopropanesulfonyl)-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	510	511	A148, 154350-29-5	Y1
334	3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	513	514	A148, 3984-14-3	Y8
335	3-cyclobutyl-*N*-(ethanesulfonyl)-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	498	499	A148, 1520-70-3	Y1
336	*N*-(methanesulfonyl)-1-[2-(morpholin-4-yl)pyridin-4-yl]-4-[(oxan-4-yl)methoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	558	559	A272, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
337	ethyl 4-[1-(4-fluorophenyl)-6-[(methanesulfonyl)carbamoyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl]piperazine-1-carboxylate	532	533	A273, 3144-09-0	Y1
338	1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(3-methyl-2-oxo-1-oxa-3,8-diazaspiro[4.5]decan-8-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	545	546	A274, 3144-09-0	Y1
339	1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-4-[3-(trifluoromethyl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	528	529	A275, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
340	1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[4-(2-methoxyethyl)piperazin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	519	520	A276, 3144-09-0	Y1
341	4-(2,4-dioxo-1,3,8-triazaspiro[4.5]decan-8-yl)-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	543	544	A277, 3144-09-0	Y1
342	4-[4-(ethoxymethyl)-4-fluoropiperidin-1-yl]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	536	537	A278, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
343	4-{4-fluoro-4-[(2-methoxyethoxy)methyl]piperidin-1-yl}-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	566	567	A279, 3144-09-0	Y1
344	4-[(3*R*,4*R*)-3-fluoro-4-hydroxypiperidin-1-yl]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	493	494	A280, 3144-09-0	Y1
345	4-[4-fluoro-4-(methoxymethyl)piperidin-1-yl]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	522	523	A281, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
346	4-{3-fluoro-3-[(2-methoxyethoxy)methyl]piperidin-1-yl}-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	566	567	A282, 3144-09-0	Y1
347	3-cyclobutyl-*N*-[3-(morpholin-4-yl)propane-1-sulfonyl]-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	597	598	A148, S10	Y1 Specific example
348	4-([1,4'-*b*ipiperidin]-1'-yl)-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	543	544	A283, 3144-09-0	Y1
349	3-cyclobutyl-4-[(3*R*)-3-(hydroxymethyl)piperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	483	484	A284, 3144-09-0	Y1 Specific example

Cpd Number	Name	MW	Mes	SM	Method
350	3-cyclobutyl-4-[(3*R*)-3-(hydroxymethyl)piperidin-1-yl]-*N*-[3-(morpholin-4-yl)propane-1-sulfonyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	596	597	A284, S10	Y1 Specific example
351	3-cyclobutyl-4-[(oxan-4-yl)methoxy]-1-phenyl-*N*-[4-(pyrrolidin-1-yl)piperidine-1-sulfonyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	622	623	A148, 878388-02-4	Y8
352	3-cyclobutyl-*N*-[(2*S*)-2-(4-methylpiperazine-1-carbonyl)pyrrolidine-1-sulfonyl]-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	665	666	A148, S11	Y8
353	*N*-([1,4'-*b*ipiperidine]-1'-sulfonyl)-3-cyclobutyl-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	636	637	A148, 1057107-11-5	Y8

Cpd Number	Name	MW	Mes	SM	Method
354	3-cyclobutyl-*N*-[methyl(propyl)sulfamoyl]-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	541	542	A148, 1094790-34-7	Y8
355	3-cyclobutyl-*N*-[ethyl(propyl)sulfamoyl]-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	555	556	A148, 1094866-01-9	Y8
356	ethyl 4-[({3-cyclobutyl-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)amino]piperidine-1-carboxylate	640	641	A148, 1707598-61-5	Y8
357	*N*-(4-acetyl-1,4-diazepane-1-sulfonyl)-3-cyclobutyl-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	610	611	A148, 1565521-97-2	Y8

Cpd Number	Name	MW	Mes	SM	Method
358	3-cyclobutyl-*N*-(morpholine-4-sulfonyl)-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	555	556	A148, 25999-04-6	Y8
359	3-cyclobutyl-*N*-[4-(morpholin-4-yl)piperidine-1-sulfonyl]-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	638	639	A148, 1057107-09-1	Y8
360	3-cyclobutyl-*N*-[4-(4-methylpiperazine-1-carbonyl)piperidine-1-sulfonyl]-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	679	680	A148, S12	Y8
361	3-cyclobutyl-*N*-(4-methylpiperazine-1-sulfonyl)-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	568	569	A148, 29604-19-1	Y8

Cpd Number	Name	MW	Mes	SM	Method
362	3-cyclobutyl-*N*-(2-methylpropane-2-sulfonyl)-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	526	527	A148, 34813-49-5	Y1
363	4-(4-azidophenyl)-*N*-(but-3-yne-1-sulfonyl)-1-[3-(dimethylamino)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	557	558	A238, 1341659-00-4	Y1
364	*N*-(cyanomethanesulfonyl)-3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	522	523	A136, S3	Y1
365	4-([1,4'-*b*ipiperidin]-1'-yl)-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	536	537	A081	Y1 Specific example

Cpd Number	Name	MW	Mes	SM	Method
366	3-cyclobutyl-*N*-(2-hydroxyethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	527	528	AC05	Y6 Specific example
367	3-cyclobutyl-*N*-(3-hydroxypropane-1-sulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	541	542	AC04	Y6
368	3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-*N*-(piperidine-4-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	566	567	AC03	Y6 Specific example
369	3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-(oxolane-3-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	553	554	A136, S4	Y1

Cpd Number	Name	MW	Mes	SM	Method
370	1-(2,6-dimethylpyridin-4-yl)-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	514	515	A236, 3144-09-0	Y1
371	3-cyclobutyl-4-(1,1-dioxo-1λ^6,4-thiazinan-4-yl)-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	503	504	A209, 3144-09-0	Y1
372	3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-*N*-[2-(1*H*-pyrazol-1-yl)ethanesulfonyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	577	578	A136	Y1
373	benzyl [2-({3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)ethyl]carbamate	660	661	A136, S5	Y1

Cpd Number	Name	MW	Mes	SM	Method
374	3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-(1-methylcyclopropane-1-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	537	538	A136, 669008-26-8	Y1
375	3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-(2-methylpropane-1-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	539	540	A136, 60199-80-6	Y1
376	methyl ({3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)acetate	555	556	A136, S6	Y1

Cpd Number	Name	MW	Mes	SM	Method
377	benzyl 3-({3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)pyrrolidine-1-carboxylate	686	687	A136, S7	Y1
378	*tert*-butyl 4-[1-(4-fluorophenyl)-6-[(methanesulfonyl)carbamoyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl]piperidine-1-carboxylate	559	560	A244, 3144-09-0	Y1
379	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[2-(methoxymethyl)morpholin-4-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	629	630	A286, 3984-14-3	Y8 Specific example

Cpd Number	Name	MW	Mes	SM	Method
380	3-cyclobutyl-*N*-(morpholine-4-sulfonyl)-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	607	608	A285, 25999-04-6	Y8, Specific example
381	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	613	614	A288	Y8
382	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[4-(propan-2-yl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	626	627	A287	Y8
383	3-cyclobutyl-*N*-(morpholine-4-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	609	610	A268	Y5 Specific example

Cpd Number	Name	MW	Mes	SM	Method
384	*N*-(2-amino-2-oxoethanesulfonyl)-3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	540	541	A136	Y1
385	3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-(2-methoxypyridin-4-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	528	529	A315	Y1
386	*N*-(2-acetamidoethanesulfonyl)-3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	568	569	AC08	Specific example
387	3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-*N*-(pyrrolidine-3-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	552	553	AC09	Specific example

Cpd Number	Name	MW	Mes	SM	Method
388	3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-*N*-[4-(pyrrolidin-1-yl)piperidine-1-sulfonyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	635	636	A136, 878388-02-4	Y8, Specific example
389	3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[(2*S*)-2-(4-methylpiperazine-1-carbonyl)pyrrolidine-1-sulfonyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	678	679	A136, S11	Y8
390	3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-{4-[(2*S*)-2-(methoxymethyl)pyrrolidin-1-yl]piperidine-1-sulfonyl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	679	680	A136	Y8

Cpd Number	Name	MW	Mes	SM	Method
391	3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[methyl(propyl)sulfamoyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	554	555	A136, 25855-60-1	Y8
392	3-cyclobutyl-*N*-[ethyl(propyl)sulfamoyl]-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	568	569	A136, 1094523-71-3	Y8
393	ethyl 4-[({3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)amino]piperidine-1-carboxylate	653	654	A136, 1707598-61-5	Y8

Cpd Number	Name	MW	Mes	SM	Method
394	*N*-(4-acetyl-1,4-diazepane-1-sulfonyl)-3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	623	624	A136, 1565521-97-2	Y8
395	3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-{4-[(2*R*)-2-(methoxymethyl)pyrrolidin-1-yl]piperidine-1-sulfonyl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	679	680	A136	Y8
396	3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-(morpholine-4-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	568	569	A136, 25999-04-6	Y8
397	3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[4-(morpholin-4-yl)piperidine-1-sulfonyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	651	652	A136, 1057107-09-1	Y8

Cpd Number	Name	MW	Mes	SM	Method
398	3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[4-(4-methylpiperazine-1-carbonyl)piperidine-1-sulfonyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	692	693	A136, S12	Y8
399	3-cyclobutyl-*N*-(4-fluoropiperidine-1-sulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	584	585	A136, 1228338-35-9	Y8
400	3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-(4-methylpiperazine-1-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	581	582	A136, 29604-19-1	Y8
401	3-cyclobutyl-*N*-(cyclopropanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	523	524	A136, 154350-29-5	Y1

Cpd Number	Name	MW	Mes	SM	Method
402	3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	526	527	A136, 3984-14-3	Y8
403	3-cyclobutyl-*N*-(ethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	511	512	A136, 1520-70-3	Y1
404	1-cyclohexyl-*N*-(methanesulfonyl)-4-{4-[(morpholin-4-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	556	556	A380, 3144-09-0	Y1
405	1-cyclohexyl-*N*-(2-methoxyethanesulfonyl)-4-{4-[(morpholin-4-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	600	600	A380, 51517-04-5	Y1

Cpd Number	Name	MW	Mes	SM	Method
406	1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[(morpholin-4-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	585	585	A380, 3984-14-3	Y8
407	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(2-methoxyethanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	601	602	A308, 51517-04-5	Y1
408	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	585	586	A308, [3984-14-3]	Y8
409	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[(morpholin-4-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	599	600	A404, [3984-14-3]	Y8

Cpd Number	Name	MW	Mes	SM	Method
410	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-{4-[(morpholin-4-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	570	571	A404, [3144-09-0]	Y1
411	1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	544	545	A408, 3144-09-0	Y1 Specific example
412	*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	573	574	A408, 3984-14-3	Y8 Specific example
413	*N*-(ethanesulfonyl)-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	558	559	A408, 1520-70-3	Y1 Specific example

Cpd Number	Name	MW	Mes	SM	Method
414	*N*-(cyclopropanesulfonyl)-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	570	569 $(M-H)^-$ (ESI-)	A408, 154350-29-5	Y1 Specific example
415	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(2-methoxyethanesulfonyl)-4-{4-[2-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	629	630	A311, [51517-04-5]	Y1
416	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[2-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	614	615	A311, [3984-14-3]	Y8

Cpd Number	Name	MW	Mes	SM	Method
417	3-cyclobutyl-*N*-[(1,4-dioxan-2-yl)methanesulfonyl]-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	583	584	A136	Y1
418	3-cyclobutyl-1-cyclohexyl-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	545	545	A403, [3144-09-0]	Y1
419	3-cyclobutyl-1-cyclohexyl-*N*-(2-methoxyethanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	589	589	A403, [51517-04-5]	Y1
420	3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	574	574	A403, [3984-14-3]	Y8

Cpd Number	Name	MW	Mes	SM	Method
421	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	556	557	A308	Y1
422	1-cyclohexyl-*N*-(methanesulfonyl)-4-[4-(4-methylpiperazine-1-carbonyl)phenyl]-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	583	584	A381, 3144-09-0	Y1
423	1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-[4-(4-methylpiperazine-1-carbonyl)phenyl]-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	612	613	A381, 3984-14-3	Y8

Cpd Number	Name	MW	Mes	SM	Method
424	3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[(morpholin-4-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	588	589	A401, [3984-14-3]	Y8
425	3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[2-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	602	603	A402, [3984-14-3]	Y8
426	4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	565	566	A081, 3984-14-3	Y8 Specific example
427	4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-*N*-(ethanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	550	551	A081, 1520-70-3	Y1 Specific example

Cpd Number	Name	MW	Mes	SM	Method
428	4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-*N*-(cyclopropanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	562	563	A081, 154350-29-5	Y1 Specific example
429	3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-*N*-(oxolane-3-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	612	613	A308	Y1
430	3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-(2-methylpyridin-4-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	512	513	AC10	Y1
431	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-{4-[2-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	584	585	A311	Y1

Cpd Number	Name	MW	Mes	SM	Method
432	3-cyclobutyl-*N*-[methyl(propyl)sulfamoyl]-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	595	596	A409, 25855-60-1	Y5, Specific example
433	ethyl 4-[({3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)amino]piperidine-1-carboxylate	694	695	A409, 1707598-61-5	Y5
434	3-cyclobutyl-*N*-(4-fluoropiperidine-1-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	625	626	A409, 1228338-35-9	Y5

Cpd Number	Name	MW	Mes	SM	Method
435	3-cyclobutyl-*N*-(1-methylcyclopropane-1-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	578	579	A409, 669008-26-8	Y5
436	3-cyclobutyl-*N*-(cyclopropanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	564	565	A409, 154350-29-5	Y5
437	3-cyclobutyl-*N*-(ethanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	552	553	A409, 1520-70-3	Y5 Specific example
438	3-cyclobutyl-*N*-(2-methoxyethanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	582	583	A409, 51517-04-5	Y5

Cpd Number	Name	MW	Mes	SM	Method
439	3-cyclobutyl-*N*-{4-[(2*S*)-2-(methoxymethyl)pyrrolidin-1-yl]piperidine-1-sulfonyl}-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	720	721	A409	Y5
440	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[1-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	613	614	A360, 3984-14-3	Y8
441	1-cyclohexyl-*N*-(methanesulfonyl)-4-{4-[(4-methylpiperazin-1-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	569	569	A386, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
442	1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[(4-methylpiperazin-1-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	598	598	A386, 3984-14-3	Y8
443	1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[(piperidin-1-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	583	584	A385, 3984-14-3	Y8
444	1-cyclohexyl-*N*-(dimethylsulfamoyl)-3-[(propan-2-yl)oxy]-4-{4-[(pyrrolidin-1-yl)methyl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	569	570	A387, 3984-14-3	Y8
445	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-{4-[1-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	584	585	A360, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
446	3-cyclobutyl-*N*-(ethanesulfonyl)-1-(4-fluorophenyl)-4-{4-[1-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	598	599	A360, 1520-70-3	Y1
447	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(2-methoxyethanesulfonyl)-4-{4-[(morpholin-4-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	614	615	A404, [51517-04-5]	Y1
448	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(2-hydroxyethanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	586	587	AC11	Y6
450	4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	554	555	A309	Y1

Cpd Number	Name	MW	Mes	SM	Method
451	4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-1-(4-fluorophenyl)-*N*-(oxolane-3-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	610	611	A309	Y1
452	3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[2-(morpholin-4-yl)ethyl]piperidin-1-yl}-*N*-(oxolane-3-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	640	641	A311	Y1
453	*N*-([1,4'-bipiperidine]-1'-sulfonyl)-3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	690	691	A409, 1057107-11-5	Y5
454	4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-*N*-[3-(morpholin-4-yl)propane-1-sulfonyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	649	650	A081, 736182-77-7	Y1 Specific example

Cpd Number	Name	MW	Mes	SM	Method
455	3-cyclobutyl-*N*-(4-methylpiperazine-1-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	622	623	A409, 29604-19-1	Y5
456	3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	567	568	A409, 3984-14-3	Y5
457	ethyl 4-{[(3-cyclobutyl-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl)sulfamoyl]amino}piperidine-1-carboxylate	692	693	A285, 1707598-61-5	Y5

Cpd Number	Name	MW	Mes	SM	Method
458	3-cyclobutyl-*N*-{4-[(2*R*)-2-(methoxymethyl)pyrrolidin-1-yl]piperidine-1-sulfonyl}-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	718	719	A285	Y5
459	3-cyclobutyl-*N*-(4-fluoropiperidine-1-sulfonyl)-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	623	624	A285, 1228338-35-9	Y5
460	3-cyclobutyl-*N*-(4-methylpiperazine-1-sulfonyl)-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	620	621	A285, 29604-19-1	Y5

Cpd Number	Name	MW	Mes	SM	Method
461	3-cyclobutyl-*N*-(1-methylcyclopropane-1-sulfonyl)-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	576	577	A285, 669008-26-8	Y5
462	3-cyclobutyl-*N*-(cyclopropanesulfonyl)-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	562	563	A285, 154350-29-5	Y5
463	3-cyclobutyl-*N*-(ethanesulfonyl)-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	550	551	A285, 1520-70-3	Y5

Cpd Number	Name	MW	Mes	SM	Method
464	3-cyclobutyl-*N*-(2-methoxyethanesulfonyl)-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	580	581	A285, 51517-04-5	Y5
465	3-cyclobutyl-*N*-(2-methylpropane-2-sulfonyl)-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	578	579	A285, 34813-49-5	Y5
466	3-cyclobutyl-*N*-(ethanesulfonyl)-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	571	571	A308, 1520-70-3	Y8

Cpd Number	Name	MW	Mes	SM	Method
467	3-(cyclobutyloxy)-1-cyclohexyl-4-{4-[(morpholin-4-yl)methyl]phenyl}-*N*-(oxolane-3-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	624	624	A383, S4	Y1
468	3-cyclobutyl-1-cyclohexyl-*N*-(oxolane-3-sulfonyl)-4-[4-(pyridin-4-yl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	594	594	A382, S4	Y1
469	3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-[4-(pyridin-4-yl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	601	602	A382, 3984-14-3	Y8
470	3-cyclobutyl-1-cyclohexyl-*N*-(ethanesulfonyl)-4-[4-(pyridin-4-yl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	552	552	A382, 1520-70-3	Y1

Cpd Number	Name	MW	Mes	SM	Method
471	3-cyclobutyl-1-(4-fluorophenyl)-*N*-[(2-methoxyethyl)(methyl)sulfamoyl]-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	630	631	A308, 508241-84-7	Y8
472	4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	583	584	A363, [3984-14-3]	Y8
473	3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-[2-(oxan-4-yl)pyridin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	582	583	A316	Y1
474	3-cyclobutyl-*N*-(methanesulfonyl)-1-(2-methoxypyridin-4-yl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	569	570	A317	Y1

Cpd Number	Name	MW	Mes	SM	Method
475	3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[(morpholin-4-yl)methyl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	580	581	A364, 3984-14-3	Y8
476	3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[2-(morpholin-4-yl)ethyl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	594	595	A365, 3984-14-3	Y8
477	*N*-(but-3-yne-1-sulfonyl)-3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	594	595	A308, 1341659-00-4	Y1
478	4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-*N*-(ethanesulfonyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	568	569	A309, 1520-70-3	Y1

Cpd Number	Name	MW	Mes	SM	Method
479	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[(1*R*)-1-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	613	614	440	Chiral separation, first eluting peak
480	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[(1*S*)-1-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	613	614	440	Chiral separation, last eluting peak
481	3-(cyclobutyloxy)-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[(morpholin-4-yl)methyl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	597	598	A383, 3984-14-3	Y8

Cpd Number	Name	MW	Mes	SM	Method
482	3-cyclobutyl-1-(4-fluorophenyl)-*N*-[methyl(propan-2-yl)sulfamoyl]-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	614	615	A308, 372136-76-0	Y8
483	3-cyclobutyl-*N*-[ethyl(methyl)sulfamoyl]-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	600	601	A308, 154743-05-2	Y8
484	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(3-methoxyazetidine-1-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	628	629	A308, 1427081-07-9	Y8

Cpd Number	Name	MW	Mes	SM	Method
485	3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-*N*-(pyrrolidine-1-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	612	613	A308, 4108-88-7	Y8
486	3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-*N*-(2,2,2-trifluoroethanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	625	626	A308, 67497-95-4	Y1
487	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(morpholine-4-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	628	629	A308, 25999-04-6	Y8

Cpd Number	Name	MW	Mes	SM	Method
488	4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-1-(4-fluorophenyl)-*N*-(2-methoxyethanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	599	599	A309, [51517-04-5]	Y1
489	*N*-(dimethylsulfamoyl)-1-[2-(morpholin-4-yl)pyridin-4-yl]-4-[(oxan-4-yl)methoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	587	588	A272	Y8
490	3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-[2-(oxan-4-yl)pyridin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	623	624	A328	Y1

Cpd Number	Name	MW	Mes	SM	Method
491	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(2-hydroxyethanesulfonyl)-4-{4-[2-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	614	615	AC12	Y6
492	methyl 4-(1-{3-cyclobutyl-6-[(dimethylsulfamoyl)carbamoyl]-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperidin-4-yl)piperazine-1-carboxylate	643	644	A399, [3984-14-3]	Y8
493	4-[4-(4-acetylpiperazin-1-yl)piperidin-1-yl]-3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	627	628	A400, [3984-14-3]	Y8

Cpd Number	Name	MW	Mes	SM	Method
494	3-cyclobutyl-*N*-(ethanesulfonyl)-1-(4-fluorophenyl)-4-{4-[(morpholin-4-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	584	585	A404, [1520-70-3]	Y1
495	3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[(morpholin-4-yl)methyl]piperidin-1-yl}-*N*-(oxolane-3-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	626	627	A404, S4	Y1
496	ethyl 4-[1-(4-fluorophenyl)-6-[(methanesulfonyl)carbamoyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl]piperidine-1-carboxylate	531	532	AC13	Y1

Cpd Number	Name	MW	Mes	SM	Method
497	ethyl 4-{6-[(dimethylsulfamoyl)carbamoyl]-1-(4-fluorophenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperidine-1-carboxylate	560	561	AC13	Y8
498	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(3-methylphenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	581	582	A318a	Y8
499	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(3-methoxyphenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	597	598	A318b	Y8

Cpd Number	Name	MW	Mes	SM	Method
500	3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-[4-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	635	636	A319	Y8
501	3-cyclobutyl-4-[4-(ethoxymethyl)-4-fluoropiperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	529	530	A338	Y1
502	3-cyclobutyl-4-{4-fluoro-4-[(2-methoxyethoxy)methyl]piperidin-1-yl}-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	559	560	A339	Y1

Cpd Number	Name	MW	Mes	SM	Method
503	3-cyclobutyl-4-{3-fluoro-3-[(2-methoxyethoxy)methyl]piperidin-1-yl}-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	559	560	A340	Y1
504	3-cyclobutyl-4-[4-fluoro-4-(methoxymethyl)piperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	515	516	A341	Y1
505	*N*-(4-cyanopiperidine-1-sulfonyl)-3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	650	651	A308	Y8

Cpd Number	Name	MW	Mes	SM	Method
506	3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-*N*-(oxetane-3-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	599	599	A308, 1335234-13-3	Y1
507	3-cyclobutyl-*N*-(cyclopropanesulfonyl)-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	582	583	A308	Y1
508	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(1-methylcyclopropane-1-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	596	597	A308	Y1
509	3-cyclobutyl-*N*-(methanesulfonyl)-1-(3-methylphenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	552	553	A318a	Y1

Cpd Number	Name	MW	Mes	SM	Method
510	3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-[4-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	606	607	A319	Y1
511	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluoro-3-methylphenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	599	600	A320	Y8
512	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(3-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	585	586	A326	Y8

Cpd Number	Name	MW	Mes	SM	Method
513	3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	635	636	A321	Y8
514	3-cyclobutyl-1-(4-fluoro-3-methylphenyl)-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	570	571	A320	Y1
515	3-cyclobutyl-1-(3-fluorophenyl)-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	556	557	A326	Y1

Cpd Number	Name	MW	Mes	SM	Method
516	3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	606	607	A321	Y1
517	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	572	573	AC16	Y9 Specific example
518	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[(4-methylpiperazin-1-yl)methyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	501	501	A390, 3144-09-0	Y1
519	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[(morpholin-4-yl)methyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	488	488	A389, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
520	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[(morpholin-4-yl)methyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	517	517	A389, 3984-14-3	Y8
521	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{[4-(methoxymethyl)piperidin-1-yl]methyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	559	559	A388, 3984-14-3	Y8
522	4-(4-cyano[1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	608	609	A391, 3984-14-3	Y8
523	4-[4-(3-cyanoazetidin-1-yl)piperidin-1-yl]-3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	580	581	A357	Y8

Cpd Number	Name	MW	Mes	SM	Method
524	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[4-(3-methoxypyrrolidin-1-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	599	600	A358	Y8
525	3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-(4-fluoro[1,4'-bipiperidin]-1'-yl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	587	588	A306	Y8
526	3-cyclobutyl-4-(4,4-difluoro[1,4'-bipiperidin]-1'-yl)-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	619	620	A289	Y8
527	4-[4-(2-cyanomorpholin-4-yl)piperidin-1-yl]-3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	610	611	A290	Y8

Cpd Number	Name	MW	Mes	SM	Method
528	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[methyl(oxan-4-yl)amino]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	613	614	A292	Y8
529	3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-{2-[(propan-2-yl)oxy]pyridin-4-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	626	627	A322	Y8
530	3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-{2-[(propan-2-yl)oxy]pyridin-4-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	597	598	A322	Y1

Cpd Number	Name	MW	Mes	SM	Method
531	3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-[2-(oxan-4-yl)pyridin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	582	583	A316	Y8
532	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[4-(2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	597	598	A291	Y8
533	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[3-(morpholin-4-yl)-1-oxa-8-azaspiro[4.5]decan-8-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	641	642	A310	Y8

Cpd Number	Name	MW	Mes	SM	Method
534	1-cyclohexyl-*N*-(dimethylsulfamoyl)-3-[(propan-2-yl)oxy]-4-{4-[4-(propan-2-yl)piperazin-1-yl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	611	612	A395, 3984-14-3	Y8
535	3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-[4-(2-methylpyridin-4-yl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	508	581	A366, 3984-14-3	Y8
536	3-cyclobutyl-1-cyclohexyl-4-[6-(4-cyclopropylpiperazin-1-yl)pyridin-3-yl]-*N*-(dimethylsulfamoyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	606	607	A405, 3984-14-3	Y8

Cpd Number	Name	MW	Mes	SM	Method
537	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(3-fluoropyrrolidine-1-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	629	630	A308, S13	Y8
538	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(3-methoxypyrrolidine-1-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	641	642	A308, S14	Y8
539	4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	584	585	A056	Y8

Cpd Number	Name	MW	Mes	SM	Method
540	3-cyclobutyl-1-(4-fluorophenyl)-*N*-[4-(methoxymethyl)piperidine-1-sulfonyl]-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	669	670	A308, S15	Y8
541	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[4-(3-fluoropyrrolidin-1-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	587	588	A356	Y8
542	3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{6-[4-(propan-2-yl)piperazin-1-yl]pyridin-3-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	608	609	A406, 3984-14-3	Y8

Cpd Number	Name	MW	Mes	SM	Method
543	3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[1-(morpholin-4-yl)ethyl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	594	595	A367, 3984-14-3	Y8
544	1-cyclohexyl-4-{4-[4-(dimethylamino)piperidine-1-carbonyl]phenyl}-*N*-(methanesulfonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	611	611	A384, 3144-09-0	Y1
545	1-cyclohexyl-4-{4-[4-(dimethylamino)piperidine-1-carbonyl]phenyl}-*N*-(2-methoxyethanesulfonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	655	655	A384, 51517-04-5	Y1
546	1-cyclohexyl-4-{4-[4-(dimethylamino)piperidine-1-carbonyl]phenyl}-*N*-(dimethylsulfamoyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	640	640	A384, 3984-14-3	Y8

Cpd Number	Name	MW	Mes	SM	Method
547	3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[4-(propan-2-yl)piperazin-1-yl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	607	608	A368, 3984-14-3	Y8
548	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	584	585	A344, [3144-09-0]	Y1
549	3-cyclobutyl-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-*N*-(dimethylsulfamoyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	606	607	A313	Y8

Cpd Number	Name	MW	Mes	SM	Method
550	3-cyclobutyl-*N*-(cyclopropanesulfonyl)-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	603	604	A313	Y1
551	3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-[6-(4-methylpiperazin-1-yl)pyridin-3-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	580	581	A369, 3984-14-3	Y8
552	3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{6-[4-(2-methoxyethyl)piperazin-1-yl]pyridin-3-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	624	625	A370, 3984-14-3	Y8

Cpd Number	Name	MW	Mes	SM	Method
553	3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[4-(propan-2-yl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	614	615	A371, 3984-14-3	Y8
554	3-cyclobutyl-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-*N*-[methyl(propyl)sulfamoyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	634	635	A313	Y8
555	3-cyclobutyl-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-*N*-(morpholine-4-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	648	649	A313	Y8
556	3-cyclobutyl-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	577	578	A313	Y1

Cpd Number	Name	MW	Mes	SM	Method
557	3-cyclobutyl-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-*N*-(1-methylcyclopropane-1-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	617	618	A313	Y1
558	3-cyclobutyl-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-*N*-(methylsulfamoyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	592	593	A313	Y8
559	1-cyclohexyl-4-[4-(4-cyclopropylpiperazin-1-yl)phenyl]-*N*-(dimethylsulfamoyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	609	610	A393, 3984-14-3	Y8
560	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[3-(trifluoromethyl)pyrrolidin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	637	638	A293	Y8

Cpd Number	Name	MW	Mes	SM	Method
561	4-[4-(3-cyanopyrrolidin-1-yl)piperidin-1-yl]-3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	594	595	A294	Y8
562	4-(3-cyano[1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	608	609	A295	Y8
563	3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-(3-fluoro[1,4'-bipiperidin]-1'-yl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	601	602	A296	Y8

Cpd Number	Name	MW	Mes	SM	Method
564	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-{4-[3-(trifluoromethyl)pyrrolidin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	608	609	A293	Y1
565	4-[4-(3-cyanopyrrolidin-1-yl)piperidin-1-yl]-3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	565	566	A294	Y1
566	4-(3-cyano[1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	579	580	A295	Y1
567	3-cyclobutyl-4-(3-fluoro[1,4'-bipiperidin]-1'-yl)-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	572	573	A296	Y1

Cpd Number	Name	MW	Mes	SM	Method
568	3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-*N*-(piperidine-1-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	625	625	A308, S16	Y8
569	3-cyclobutyl-*N*-(3-fluoroazetidine-1-sulfonyl)-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	615	616	A308, S17	Y8
570	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[4-(3-methoxyazetidin-1-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	585	586	A297	Y8

Cpd Number	Name	MW	Mes	SM	Method
571	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[3-(trifluoromethyl)[1,4'-bipiperidin]-1'-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	651	652	A298	Y8
572	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-(3-methoxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	613	614	A299	Y8
573	3-cyclobutyl-4-[4-(2,2-dimethylmorpholin-4-yl)piperidin-1-yl]-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	613	614	A300	Y8
574	*N*-(2-acetamidoethanesulfonyl)-3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	627	628	A308	Y1

Cpd Number	Name	MW	Mes	SM	Method
575	3-cyclobutyl-1-[2-(difluoromethoxy)pyridin-4-yl]-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	634	635	A325	Y8
576	*N*-(azetidine-1-sulfonyl)-3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	597	598	A308, S18	Y8
577	3-cyclobutyl-1-(4-fluorophenyl)-*N*-[(2*R*)-2-(methoxymethyl)pyrrolidine-1-sulfonyl]-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	655	656	A308, S19	Y8

Cpd Number	Name	MW	Mes	SM	Method
578	3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-*N*-[(oxan-4-yl)sulfamoyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	641	642	A308, S20	Y8
579	3-cyclobutyl-1-(4-fluorophenyl)-*N*-[methyl(oxan-4-yl)sulfamoyl]-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	655	656	A308, S21	Y8
580	3-cyclobutyl-*N*-(3,3-difluoroazetidine-1-sulfonyl)-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	633	634	A308, S22	Y8

Cpd Number	Name	MW	Mes	SM	Method
581	4-[(3*S*)-4-benzyl-3-methylpiperazin-1-yl]-3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	593	594	A372, 3984-14-3	Y8
582	4-[(3*R*)-4-benzyl-3-methylpiperazin-1-yl]-3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	593	594	A373, 3984-14-3	Y8
583	3-cyclobutyl-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	624	625	A374, 3984-14-3	Y8
584	3-cyclobutyl-4-(9-cyclopropyl-3,9-diazaspiro[5.5]undecan-3-yl)-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	609	610	A375, 3984-14-3	Y8

Cpd Number	Name	MW	Mes	SM	Method
585	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[4-(3-methoxyazetidin-1-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	556	557	A297	Y1
586	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[3-(trifluoromethyl)[1,4'-bipiperidin]-1'-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	622	623	A298	Y1
587	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(3-methoxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	584	585	A299	Y1
588	3-cyclobutyl-4-[4-(2,2-dimethylmorpholin-4-yl)piperidin-1-yl]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	584	585	A300	Y1

Cpd Number	Name	MW	Mes	SM	Method
589	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	583	584	A376, 3984-14-3	Y8
590	ethyl 4-(1-{3-cyclobutyl-6-[(dimethylsulfamoyl)carbamoyl]-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperidin-4-yl)piperazine-1-carboxylate	656	657	A301	Y8
591	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[(2-methoxyethyl)(methyl)amino]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	587	588	A307	Y8

Cpd Number	Name	MW	Mes	SM	Method
592	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methoxysulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	587	588	A308, S23	Y8
593	3-cyclobutyl-4-[1-(4,4-difluorocyclohexyl)piperidin-4-yl]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	589	590	A329	Y1
594	3-cyclobutyl-4-[1-(4,4-difluorocyclohexyl)piperidin-4-yl]-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	618	619	A329	Y8
595	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{[4-(morpholin-4-yl)piperidin-1-yl]methyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	599	600	A361, 3984-14-3	Y8

Cpd Number	Name	MW	Mes	SM	Method
596	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-{[4-(morpholin-4-yl)piperidin-1-yl]methyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	570	571	A361, 3144-09-0	Y1
597	1-cyclohexyl-4-{4-[(4-cyclopropylpiperazin-1-yl)methyl]phenyl}-*N*-(methanesulfonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	594	595	A392, 3144-09-0	Y1
598	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[1-(propan-2-yl)piperidin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	542	543	A330	Y8
599	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[1-(oxan-4-yl)piperidin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	555	556	A331	Y1

Cpd Number	Name	MW	Mes	SM	Method
600	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-{1-[(oxan-4-yl)methyl]piperidin-4-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	569	570	A332	Y1
601	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{1-[(oxan-4-yl)methyl]piperidin-4-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	598	599	A332	Y8
602	3-cyclobutyl-4-{1-[(2,5-dimethoxyoxolan-3-yl)methyl]piperidin-4-yl}-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	615	616	A333	Y1

Cpd Number	Name	MW	Mes	SM	Method
603	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[1-(3,3,3-trifluoropropyl)piperidin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	567	568	A334	Y1
604	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[1-(3,3,3-trifluoropropyl)piperidin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	596	597	A334	Y8
605	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-(4-hydroxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	599	600	A362, [3984-14-3]	Y8
606	methyl {3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamate	572	573	A308	Y1

Cpd Number	Name	MW	Mes	SM	Method
607	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[4-(2-methoxyethyl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	642	643	A377, 3984-14-3	Y8
608	3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[3-(morpholin-4-yl)pyrrolidine-1-sulfonyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	655	656	A202, S24	Y8
609	3-cyclobutyl-*N*-(4-cyclopropylpiperazine-1-sulfonyl)-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	625	626	A202, S25	Y8

Cpd Number	Name	MW	Mes	SM	Method
610	3-cyclobutyl-1-(4-fluorophenyl)-*N*-[4-(2-methoxyethyl)piperazine-1-sulfonyl]-4-[4-(methoxymethyl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	643	644	A202, S26	Y8
611	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[1-(propan-2-yl)piperidin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	513	514	A330	Y1
612	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[1-(oxan-4-yl)piperidin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	584	585	A331	Y8
613	3-cyclobutyl-4-[1-(cyclopropylmethyl)piperidin-4-yl]-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	554	555	A336	Y8

Cpd Number	Name	MW	Mes	SM	Method
614	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[9-(oxetan-3-yl)-3,9-diazaspiro[5.5]undecan-3-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	625	626	A378, 3984-14-3	Y8
615	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[4-(oxetan-3-yl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	640	641	A379, 3984-14-3	Y8
616	3-cyclobutyl-4-[(1-cyclopropylpiperidin-4-yl)methoxy]-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	570	571	A394, 3984-14-3	Y8
617	3-cyclobutyl-4-[(1-cyclobutylpiperidin-4-yl)methoxy]-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	584	585	A398, 3984-14-3	Y8

Cpd Number	Name	MW	Mes	SM	Method
618	3-cyclobutyl-4-[(1-cyclohexylpiperidin-4-yl)methoxy]-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	612	613	A397, 3984-14-3	Y8
619	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{[1-(oxan-4-yl)piperidin-4-yl]methoxy}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	614	615	A396, 3984-14-3	Y8
620	3-cyclobutyl-4-{1-[(2,5-dimethoxyoxolan-3-yl)methyl]piperidin-4-yl}-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	644	645	A333	Y8

Cpd Number	Name	MW	Mes	SM	Method
621	3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-{2-[(propan-2-yl)oxy]pyrimidin-4-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	627	628	A342	Y8
622	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(2-ethoxypyrimidin-4-yl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	613	614	A343	Y8
623	3-cyclobutyl-1-(2,2-difluoro-2*H*-1,3-benzodioxol-5-yl)-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	647	648	A327	Y8

Cpd Number	Name	MW	Mes	SM	Method
624	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(4-methylpiperazine-1-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	640	641	A308	Y8
625	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[1-(propan-2-yl)octahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	583	584	A302	Y8
626	3-cyclobutyl-4-(1-cyclobutyloctahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl)-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	595	596	A303	Y8

Cpd Number	Name	MW	Mes	SM	Method
627	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[1-(oxetan-3-yl)octahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	597	598	A304	Y8
628	3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[1-(oxan-4-yl)octahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	625	626	A305	Y8
629	3-cyclobutyl-1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-*N*-(methylsulfamoyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	599	600	A344	Y8

Cpd Number	Name	MW	Mes	SM	Method
630	3-cyclobutyl-1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-*N*-sulfamoyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	585	586	A344	Y8
631	1-cyclohexyl-4-[4-(hexahydropyrrolo[3,4-*c*]pyrrole-2(1*H*)-carbonyl)phenyl]-*N*-(methanesulfonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	594	595	AC15	Y6 Specific example
632	*N*-(azetidine-1-sulfonyl)-3-cyclobutyl-1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	625	626	A344, S18	Y8
633	1-cyclohexyl-4-(4-{[3-(dimethylamino)azetidin-1-yl]methyl}phenyl)-*N*-(methanesulfonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	568	569	A411	Y1

Cpd Number	Name	MW	Mes	SM	Method
634	1-cyclohexyl-*N*-(methanesulfonyl)-3-[(propan-2-yl)oxy]-4-(4-{[4-(propan-2-yl)piperazin-1-yl]methyl}phenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	596	597	A347	Y1
635	1-cyclohexyl-*N*-(methanesulfonyl)-4-{4-[(4-methoxypiperidin-1-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	583	584	A348	Y1
636	1-cyclohexyl-*N*-(methanesulfonyl)-4-{4-[(5-methylhexahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	594	595	A349	Y1

Cpd Number	Name	MW	Mes	SM	Method
637	1-cyclohexyl-*N*-(methanesulfonyl)-4-[4-(5-methylhexahydropyrrolo[3,4-*c*]pyrrole-2(1*H*)-carbonyl)phenyl]-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	608	609	A352	Y1
638	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methylsulfamoyl)-4-{4-[4-(propan-2-yl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	612	613	A346	Y8
639	4-[4-(4-cyano-1-methylpiperidin-4-yl)phenyl]-1-cyclohexyl-*N*-(methanesulfonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	578	579	A355	Y1

Cpd Number	Name	MW	Mes	SM	Method
640	1-cyclohexyl-4-{4-[3-(dimethylamino)azetidine-1-carbonyl]phenyl}-*N*-(methanesulfonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	582	583	A353	Y1
641	1-cyclohexyl-*N*-(methanesulfonyl)-4-{4-[(8-methyl-2-oxa-5,8-diazaspiro[3.5]nonan-5-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	610	611	A354	Y1
642	1-cyclohexyl-4-{4-[(4-ethylpiperazin-1-yl)methyl]phenyl}-*N*-(methanesulfonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	582	583	AC14	I34
643	1-cyclohexyl-4-(4-{[4-(dimethylamino)piperidin-1-yl]methyl}phenyl)-*N*-(methanesulfonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	596	597	AC14	I34

Cpd Number	Name	MW	Mes	SM	Method
644	1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	588	589	A412	Y1
645	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(3-methoxyazetidine-1-sulfonyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	656	657	A344, S27	Y8
646	3-cyclobutyl-*N*-(3-fluoroazetidine-1-sulfonyl)-1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	644	645	A344, S17	Y8

Cpd Number	Name	MW	Mes	SM	Method
647	3-cyclobutyl-1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-*N*-(morpholine-4-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	655	656	A344, S28	Y8
648	3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)cyclohexyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	537	538	A345	Y1
649	3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)cyclohexyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	566	567	A345	Y8
650	3-cyclobutyl-4-(4-fluoro[1,4'-bipiperidin]-1'-yl)-1-(4-fluorophenyl)-*N*-(methylsulfamoyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	587	588	A306	Y8

Cpd Number	Name	MW	Mes	SM	Method
651	*N*-(azetidine-1-sulfonyl)-3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[4-(propan-2-yl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	638	639	A346, S18	Y8
652	3-cyclobutyl-1-[3-(difluoromethoxy)phenyl]-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	633	634	A410	Y8, Specific example
654	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-*N*-methyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	571	572	A308, 1184-85-6	Y1
656	3-cyclobutyl-*N*-(methanesulfonyl)-*N*-methyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	552	553	328	Y10, Specific example

Cpd Number	Name	MW	Mes	SM	Method
657	3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	511	512	185	Y10, Specific example
658	3-cyclobutyl-*N*-(ethanesulfonyl)-*N*-methyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	566	567	A409, 6601-37-2	Y1, Specific example
659	3-cyclobutyl-*N*-(ethanesulfonyl)-*N*-methyl-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	564	565	A285, 6601-37-2	Y1
660	2-(3-cyclobutyl-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl)-6-methyl-1λ^6,2,6-thiadiazinane-1,1-dione	591	592	A285, 137830-77-4	Y1

Cpd Number	Name	MW	Mes	SM	Method
661	2-(3-cyclobutyl-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl)-1λ^6,2-thiazolidine-1,1-dione	562	563	A285, 5908-62-3	Y1
662	3-cyclobutyl-*N*-(methanesulfonyl)-*N*-methyl-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	550	551	A285, 1184-85-6	Y1
663	2-(3-cyclobutyl-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl)-1λ^6,2-thiazinane-1,1-dione	576	577	A285, 37441-50-2	Y1
664	2-{3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}-6-methyl-1λ^6,2,6-thiadiazinane-1,1-dione	593	594	A409, 137830-77-4	Y1

Cpd Number	Name	MW	Mes	SM	Method
665	2-{3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}-1λ^6,2-thiazolidine-1,1-dione	564	565	A409, 5908-62-3	Y1
666	2-{3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}-1λ^6,2-thiazinane-1,1-dione	578	579	A409, 37441-50-2	Y1
667	2-{3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}-1λ^6,2-thiazolidine-1,1-dione	523	524	A136, 5908-62-3	Y1
668	2-{3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}-1λ^6,2-thiazinane-1,1-dione	537	538	A136, 37441-50-2	Y1

Cpd Number	Name	MW	Mes	SM	Method
669	3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-(methylsulfamoyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	530	531	A202, 72179-84-1	Y8
670	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(2-methoxyethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	559	560	A202, 51517-04-5	Y1
671	3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-(morpholine-4-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	586	587	A202, 25999-04-6	Y8

Cpd Number	Name	MW	Mes	SM	Method
672	3-cyclobutyl-1-(4-fluorophenyl)-*N*-(3-hydroxypropane-1-sulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	559	560	AC17	Y6
673	ethyl 4-[({3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)amino]piperidine-1-carboxylate	671	672	A202, 1707598-61-5	Y8
674	3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[(oxetan-3-yl)sulfamoyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	572	573	A202, 1384876-01-0	Y8

Cpd Number	Name	MW	Mes	SM	Method
675	3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[(oxan-4-yl)sulfamoyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	600	601	A202, 1566818-36-7	Y8
676	3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[4-(morpholin-4-yl)piperidine-1-sulfonyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	669	670	A202, 1057107-09-1	Y8
677	ethyl 4-{3-cyclobutyl-1-(4-fluorophenyl)-6-[(2-methoxyethanesulfonyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperazine-1-carboxylate	588	589	A415, 51517-04-5	Y1
678	ethyl 4-{3-cyclobutyl-1-(4-fluorophenyl)-6-[(morpholine-4-sulfonyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperazine-1-carboxylate	615	616	A415, 25999-04-6	Y8

Cpd Number	Name	MW	Mes	SM	Method
679	ethyl 4-{3-cyclobutyl-1-(4-fluorophenyl)-6-[(methanesulfonyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperazine-1-carboxylate	544	545	A415, 3144-09-0	Y1
680	ethyl 4-{3-cyclobutyl-1-(4-fluorophenyl)-6-[(methylsulfamoyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperazine-1-carboxylate	559	560	A415, 72179-84-1	Y8
681	2-methylpropyl 4-{3-cyclobutyl-1-(4-fluorophenyl)-6-[(methanesulfonyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperazine-1-carboxylate	572	573	A416, 3144-09-0	Y1

Cpd Number	Name	MW	Mes	SM	Method
682	2-methylpropyl 4-{3-cyclobutyl-1-(4-fluorophenyl)-6-[(morpholine-4-sulfonyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperazine-1-carboxylate	643	644	A416, 25999-04-6	Y8
683	2-methylpropyl 4-{3-cyclobutyl-1-(4-fluorophenyl)-6-[(2-methoxyethanesulfonyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperazine-1-carboxylate	616	617	A416, 51517-04-5	Y1
684	2-methylpropyl 4-{3-cyclobutyl-1-(4-fluorophenyl)-6-[(methylsulfamoyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperazine-1-carboxylate	587	588	A416, 72179-84-1	Y8

Cpd Number	Name	MW	Mes	SM	Method
685	3-cyclobutyl-1-(4-fluorophenyl)-4-(9-methyl-3,9-diazaspiro[5.5]undecan-3-yl)-*N*-(morpholine-4-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	625	626	A414, 25999-04-6	Y8
686	*N*-(2-aminopyridine-3-sulfonyl)-3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide	593	594	A202, 54136-36-6	Y1

Table XVI. ^{1}**H NMR Data of Representative Compounds**

Cpd Number	^{1}H NMR data
2	(400 MHz, $CDCl_3$) δ ppm 8.17 - 8.25 (m, 2 H), 8.02 - 8.10 (m, 2 H), 7.91 (s, 1 H), 7.49 - 7.69 (m, 5 H), 7.36 - 7.46 (m, 3 H), 7.02 (d, *J*=8.8 Hz, 2 H), 3.87 - 3.96 (m, 4 H), 3.23 - 3.35 (m, 4 H), 2.43 (s, 3 H)
3	(400 MHz, $CDCl_3$) δ ppm 8.10 (s, 1 H), 7.52 - 7.64 (m, 2 H), 7.49 (d, *J*=8.3 Hz, 3 H), 7.07 (d, *J*=8.6 Hz, 2 H), 6.85 - 7.01 (m, 2 H), 3.84 - 4.03 (m, 4 H), 3.25 - 3.43 (m, 4 H), 2.46 (s, 3 H)

Cpd Number	^{1}H NMR data
9	(300 MHz, $CDCl_3$) δ ppm 10.17 (s, 1 H), 8.47 (s, 2 H), 7.81 (s, 1 H), 3.48 (s, 3 H), 3.31 (s, 6 H), 3.16 (quin, *J*=6.7 Hz, 1 H), 1.60 - 2.22 (m, 10 H), 1.29 - 1.52 (m, 1 H), 1.22 (d, *J*=6.7 Hz, 6 H)
10	(400 MHz, $CDCl_3$) δ ppm 7.96 (s, 1 H), 7.41 - 7.47 (m, 2 H), 7.36 - 7.40 (m, 2 H), 7.25 - 7.27 (m, 1 H), 7.01 - 7.08 (m, 2 H), 6.41 - 6.49 (m, 1 H), 4.02 (t, *J*=7.3 Hz, 4 H), 3.89 - 3.97 (m, 4 H), 3.43 (s, 3 H), 3.28 - 3.34 (m, 4 H), 3.21 (quin, *J*=6.8 Hz, 1 H), 2.45 (quin, *J*=7.3 Hz, 2 H), 1.21 (d, *J*=6.8 Hz, 6 H)
11	(400 MHz, $CDCl_3$) δ ppm 10.15 (br. s., 1 H), 8.48 (s, 2 H), 7.82 (s, 1 H), 4.82 - 4.93 (m, 1 H), 3.89 - 3.97 (m, 4 H), 3.78 - 3.89 (m, 4 H), 3.48 (s, 3 H), 3.14 (quin, *J*=6.7 Hz, 1 H), 2.03 - 2.18 (m, 2 H), 1.91 - 2.03 (m, 4 H), 1.76 - 1.88 (m, 1 H), 1.57 - 1.70 (m, 2 H), 1.35 - 1.47 (m, 1 H), 1.24 (d, *J*=1.0 Hz, 6 H)
12	(400 MHz, $CDCl_3$) δ ppm 10.17 (br. s., 1 H), 8.17 (d, *J*=2.0 Hz, 1 H), 7.74 (s, 1 H), 7.48 (dd, *J*=8.7, 2.6 Hz, 1 H), 6.73 (d, *J*=8.5 Hz, 1 H), 5.46 (quin, *J*=7.2 Hz, 1 H), 3.83 - 3.92 (m, 4 H), 3.57 - 3.65 (m, 4 H), 3.46 (s, 3 H), 2.09 - 2.25 (m, 4 H), 1.95 - 2.09 (m, 2 H), 1.73 - 1.90 (m, 2 H), 1.20 (s, 9 H)
13	(300 MHz, $CDCl_3$) δ ppm 10.06 (br. s., 1 H), 7.90 - 8.06 (m, 2 H), 7.51 - 7.61 (m, 2 H), 7.46 (s, 1 H), 7.36 (tt, *J*=1.0 Hz, 1 H), 3.42 (s, 3 H), 3.31 - 3.39 (m, 4 H), 2.76 (s, 3 H), 1.79 - 1.91 (m, 4 H), 1.67 - 1.79 (m, 2 H)
14	(400 MHz, $CDCl_3$) δ ppm 10.05 (s, 1 H), 7.93 - 8.17 (m, 3 H), 7.60 (t, *J*=8.0 Hz, 2 H), 7.44 - 7.51 (m, 2 H), 7.42 (t, *J*=1.0 Hz, 1 H), 7.06 - 7.12 (m, 2 H), 3.93 (s, 3 H), 3.45 (s, 3 H), 2.42 (s, 3 H)

Cpd Number	^{1}H NMR data
15	(400 MHz, $CDCl_3$) δ ppm 9.91 (br. s., 1 H), 8.05 (dd, *J*=8.6, 1.1 Hz, 2 H), 8.01 (s, 1 H), 7.56 - 7.63 (m, 2 H), 7.44 - 7.51 (m, 2 H), 7.37 - 7.44 (m, 1 H), 7.05 - 7.13 (m, 2 H), 3.93 (s, 3 H), 3.63 (q, *J*=7.3 Hz, 2 H), 2.42 (s, 3 H), 1.48 (t, *J*=7.4 Hz, 3 H)
16	(300 MHz, $CDCl_3$) δ ppm 10.18 (br. s., 1 H), 7.96 (s, 1 H), 7.35 - 7.48 (m, 3 H), 7.27 - 7.33 (m, 2 H), 7.05 (d, *J*=8.8 Hz, 2 H), 6.57 (dd, *J*=8.1, 1.6 Hz, 1 H), 3.86 - 3.99 (m, 4 H), 3.37 - 3.48 (m, 7 H), 3.28 - 3.35 (m, 4 H), 3.22 (quin, *J*=13.6 Hz, 1 H), 2.05 - 2.12 (m, 4 H), 1.21 (d, *J*=6.7 Hz, 6 H)
17	(400 MHz, $CDCl_3$) δ ppm 9.98 (br. s., 1 H), 8.83 (d, *J*=2.2 Hz, 1 H), 8.18 (dd, *J*=8.9, 2.7 Hz, 1 H), 7.99 (s, 1 H), 7.39 - 7.46 (m, 2 H), 6.97 (d, *J*=8.9 Hz, 1 H), 6.81 - 6.88 (m, 2 H), 4.04 (s, 3 H), 3.44 (s, 3 H), 3.31 (quin, *J*=6.8 Hz, 1 H), 3.09 (s, 6 H), 1.21 (d, *J*=6.8 Hz, 6 H)
18	(400 MHz, $CDCl_3$) δ ppm 10.02 (br. s., 1 H), 8.08 (d, *J*=2.0 Hz, 1 H), 8.02 (s, 1 H), 7.90 (dd, *J*=8.2, 2.2 Hz, 1 H), 7.42 - 7.50 (m, 3 H), 7.06 - 7.12 (m, 2 H), 3.93 (s, 3 H), 3.46 (s, 3 H), 2.47 (s, 3 H), 2.41 (s, 3 H)
19	(300 MHz, $CDCl_3$) δ ppm 9.91 (br. s., 1 H), 7.90 - 8.05 (m, 2 H), 7.50 - 7.63 (m, 2 H), 7.46 (s, 1 H), 7.31 - 7.42 (m, 1 H), 3.60 (q, *J*=7.4 Hz, 2 H), 3.29 - 3.43 (m, 4 H), 2.76 (s, 3 H), 1.79 - 1.95 (m, 4 H), 1.68 - 1.79 (m, 2 H), 1.46 (t, *J*=7.5 Hz, 3 H)
20	(400 MHz, $CDCl_3$) δ ppm 10.01 (s, 1 H), 8.52 (s, 2 H), 8.03 - 8.10 (m, 2 H), 7.95 (s, 1 H), 7.57 - 7.66 (m, 2 H), 7.36 - 7.46 (m, 1 H), 3.92 - 4.01 (m, 4 H), 3.80 - 3.89 (m, 4 H), 3.45 (s, 3 H), 3.23 (quin, *J*=6.8 Hz, 1 H), 1.31 (d, *J*=6.8 Hz, 6 H)

Cpd Number	^{1}H NMR data
21	(400 MHz, $CDCl_3$) δ ppm 9.96 (s, 1 H), 8.04 (s, 1 H), 7.84 - 7.98 (m, 2 H), 7.45 (d, *J*=8.7 Hz, 2 H), 7.38 (q, *J*=8.8 Hz, 1 H), 7.06 (d, *J*=8.7 Hz, 2 H), 3.89 - 3.95 (m, 4 H), 3.46 (s, 3 H), 3.29 - 3.34 (m, 4 H), 2.44 (s, 3 H)
22	(400 MHz, $CDCl_3$) δ ppm 8.31 (d, *J*=2.4 Hz, 1 H), 7.83 (s, 1 H), 7.60 (dd, *J*=8.8, 2.5 Hz, 1 H), 6.64 (d, *J*=8.9 Hz, 1 H), 4.72 - 5.01 (m, 1 H), 3.47 (s, 3 H), 3.14 - 3.24 (m, 7 H), 2.04 - 2.20 (m, 2 H), 1.91 - 2.04 (m, 4 H), 1.77 - 1.88 (m, 1 H), 1.50 - 1.68 (m, 2 H), 1.30 - 1.48 (m, 1 H), 1.17 (d, *J*=6.8 Hz, 6 H)
23	(400 MHz, $CDCl_3$) δ ppm 9.93 (s, 1 H), 8.06 (s, 1 H), 7.74 - 7.84 (m, 2 H), 7.42 - 7.48 (m, 2 H), 7.03 - 7.09 (m, 2 H), 6.82 (tt, *J*=8.7, 2.4 Hz, 1 H), 3.89 - 3.95 (m, 4 H), 3.48 (s, 3 H), 3.29 - 3.36 (m, 4 H), 2.44 (s, 3 H)
24	(400 MHz, $CDCl_3$) δ ppm 10.13 (s, 1 H), 7.99 (s, 1 H), 7.67 (s, 2 H), 7.44 - 7.52 (m, 2 H), 7.02 - 7.10 (m, 3 H), 3.88 - 3.98 (m, 4 H), 3.44 (s, 3 H), 3.28 - 3.36 (m, 4 H), 2.42 - 2.50 (m, 9 H)
25	(300 MHz, $CDCl_3$) δ ppm 9.96 (br. s, 1 H), 8.04 (s, 1 H), 7.83 - 8.00 (m, 2 H), 7.31 - 7.51 (m, 3 H), 6.98 - 7.13 (m, 2 H), 3.87 - 3.97 (m, 4 H), 3.46 (s, 3 H), 3.25 - 3.37 (m, 4 H), 2.44 (s, 3 H)
26	(300 MHz, $CDCl_3$) δ ppm 8.44 - 8.51 (m, 1 H), 8.33 - 8.41 (m, 1 H), 8.06 (s, 1 H), 7.67 - 7.77 (m, 1 H), 7.58 - 7.67 (m, 1 H), 7.45 (d, *J*=9.0 Hz, 2 H), 6.86 (d, *J*=9.0 Hz, 2 H), 3.46 (s, 3 H), 3.10 (s, 6 H), 2.51 (s, 3 H)
27	(300 MHz, $CDCl_3$) δ ppm 10.09 (s, 1 H), 8.01 (s, 1 H), 7.80 - 7.92 (m, 2 H), 7.43 - 7.52 (m, 3 H), 7.19 - 7.25 (m, 1 H), 7.06 - 7.12 (m, 2 H), 3.93 (s, 3 H), 3.45 (s, 3 H), 3.18 - 3.19 (m, 1 H), 2.51 (s, 3 H), 2.42 (s, 3 H)

Cpd Number	^{1}H NMR data
28	(300 MHz, $CDCl_3$) δ ppm 9.96 (s, 1 H), 8.00 (s, 1 H), 7.81 - 7.90 (m, 2 H), 7.44 - 7.54 (m, 3 H), 7.19 - 7.25 (m, 1 H), 7.03 - 7.13 (m, 2 H), 3.93 (s, 3 H), 3.62 (q, *J*=7.4 Hz, 2 H), 2.51 (s, 3 H), 2.42 (s, 3 H), 1.48 (t, *J*=1.0 Hz, 3 H)
29	(300 MHz, $CDCl_3$) δ ppm 10.07 (br. s., 1 H), 8.51 (s, 2 H), 7.93 (s, 1 H), 7.74 (t, *J*=2.2 Hz, 1 H), 7.53 - 7.59 (m, 1 H), 7.47 (t, *J*=8.2 Hz, 1 H), 6.91 - 6.97 (m, 1 H), 3.90 - 3.97 (m, 4 H), 3.44 (s, 3 H), 3.19 - 3.35 (m, 11 H), 1.30 (d, *J*=6.7 Hz, 6 H)
30	(300 MHz, $CDCl_3$) δ ppm 9.94 (br. s., 1 H), 8.51 (s, 2 H), 7.93 (s, 1 H), 7.77 (t, *J*=2.2 Hz, 1 H), 7.54 - 7.60 (m, 1 H), 7.47 (t, *J*=8.1 Hz, 1 H), 6.89 - 6.98 (m, 1 H), 3.88 - 3.99 (m, 4 H), 3.61 (q, *J*=7.3 Hz, 2 H), 3.19 - 3.37 (m, 11 H), 1.46 (t, *J*=7.5 Hz, 3 H), 1.24 - 1.37 (m, 6 H)
31	(300 MHz, $CDCl_3$) δ ppm 10.10 (br. s., 1 H), 8.34 (d, *J*=1.0 Hz, 1 H), 7.95 (s, 1 H), 7.77 (t, *J*=2.2 Hz, 1 H), 7.64 (dd, *J*=8.8, 2.3 Hz, 1 H), 7.55 - 7.61 (m, 1 H), 7.46 (t, *J*=8.1 Hz, 1 H), 6.90 - 6.97 (m, 1 H), 6.67 (d, *J*=8.8 Hz, 1 H), 3.90 - 3.98 (m, 4 H), 3.43 (s, 3 H), 3.26 - 3.34 (m, 5 H), 3.22 (s, 6 H), 1.25 (d, *J*=6.7 Hz, 6 H)
32	(300 MHz, $CDCl_3$) δ ppm 9.97 (br. s., 1 H), 8.34 (d, *J*=1.8 Hz, 1 H), 7.94 (s, 1 H), 7.79 (t, *J*=2.2 Hz, 1 H), 7.64 (dd, *J*=8.8, 2.3 Hz, 1 H), 7.55 - 7.61 (m, 1 H), 7.47 (t, *J*=1.0 Hz, 1 H), 6.89 - 6.96 (m, 1 H), 6.67 (d, *J*=8.2 Hz, 1 H), 3.90 - 3.97 (m, 4 H), 3.61 (q, *J*=7.5 Hz, 2 H), 3.25 - 3.34 (m, 5 H), 3.22 (s, 6 H), 1.46 (t, *J*=7.5 Hz, 3 H), 1.25 (d, *J*=6.7 Hz, 6 H)

Cpd Number	^{1}H NMR data
33	(300 MHz, $CDCl_3$) δ ppm 7.99 - 8.09 (m, 3 H), 7.55 - 7.64 (m, 2 H), 7.35 - 7.50 (m, 3 H), 6.80 - 6.90 (m, 2 H), 3.45 (s, 3 H), 3.09 (s, 6 H), 2.50 (s, 3 H)
34	(300 MHz, $CDCl_3$) δ ppm 10.03 (br. s., 1 H), 8.37 (d, *J*=2.3 Hz, 1 H), 8.03 - 8.12 (m, 2 H), 7.96 (s, 1 H), 7.69 (dd, *J*=8.8, 2.6 Hz, 1 H), 7.55 - 7.65 (m, 2 H), 7.36 - 7.47 (m, 1 H), 6.79 (d, *J*=8.8 Hz, 1 H), 3.85 - 3.96 (m, 4 H), 3.62 - 3.75 (m, 4 H), 3.45 (s, 3 H), 3.24 (quin, *J*=6.8 Hz, 1 H), 1.26 (d, *J*=7.0 Hz, 6 H)
35	(300 MHz, $CDCl_3$) δ ppm 9.91 (br. s., 1 H), 8.37 (d, *J*=2.1 Hz, 1 H), 8.03 - 8.13 (m, 2 H), 7.95 (s, 1 H), 7.69 (dd, *J*=8.8, 2.3 Hz, 1 H), 7.60 (t, *J*=8.1 Hz, 2 H), 7.40 (t, *J*=7.5 Hz, 1 H), 6.79 (d, *J*=8.8 Hz, 1 H), 3.82 - 3.96 (m, 4 H), 3.56 - 3.73 (m, 6 H), 3.22 (quin, *J*=13.6 Hz, 1 H), 1.47 (t, *J*=7.3 Hz, 3 H), 1.26 (d, *J*=6.7 Hz, 6 H)
36	(300 MHz, $CDCl_3$) δ ppm 10.14 (br. s., 1 H), 7.96 (s, 1 H), 7.30 - 7.48 (m, 5 H), 7.05 (d, *J*=8.8 Hz, 2 H), 6.42 - 6.50 (m, 1 H), 4.35 - 4.47 (m, 1 H), 4.23 (t, *J*=7.0 Hz, 2 H), 3.90 - 3.97 (m, 4 H), 3.80 - 3.90 (m, 2 H), 3.44 (s, 3 H), 3.39 (s, 3 H), 3.28 - 3.35 (m, 4 H), 3.21 (quin, *J*=13.7 Hz, 1 H), 1.20 (d, *J*=6.7 Hz, 6 H)
37	(300 MHz, $CDCl_3$) δ ppm 10.04 (s, 1 H), 8.40 (d, *J*=2.3 Hz, 1 H), 8.03 (d, *J*=8.5 Hz, 2 H), 8.00 (s, 1 H), 7.71 (dd, *J*=8.8, 2.3 Hz, 1 H), 7.60 (t, *J*=7.8 Hz, 2 H), 7.41 (t, *J*=7.6 Hz, 1 H), 6.80 (d, *J*=8.8 Hz, 1 H), 3.83 - 3.93 (m, 4 H), 3.62 - 3.72 (m, 4 H), 3.45 (s, 3 H), 2.52 (s, 3 H)

Cpd Number	^{1}H NMR data
38	(300 MHz, $CDCl_3$) δ ppm 10.17 (s, 1 H), 7.89 (s, 1 H), 7.41 (d, *J*=8.5 Hz, 2 H), 7.03 (d, *J*=8.8 Hz, 2 H), 4.99 - 5.15 (m, 1 H), 3.85 - 3.99 (m, 4 H), 3.47 (s, 3 H), 3.25 - 3.37 (m, 4 H), 3.15 (quin, *J*=6.7 Hz, 1 H), 2.29 - 2.57 (m, 4 H), 1.99 - 2.26 (m, 4 H), 1.13 (d, *J*=6.7 Hz, 6 H)
39	(300 MHz, $CDCl_3$) δ ppm 10.19 (s, 1 H), 7.88 (s, 1 H), 7.41 (d, *J*=8.8 Hz, 2 H), 7.03 (d, *J*=8.8 Hz, 2 H), 5.00 - 5.17 (m, 1 H), 4.01 - 4.15 (m, 2 H), 3.84 - 3.96 (m, 5 H), 3.58 (td, *J*=11.4, 2.8 Hz, 1 H), 3.46 (s, 3 H), 3.25 - 3.35 (m, 4 H), 3.14 (quin, *J*=6.8 Hz, 1 H), 2.43 (s, 1 H), 2.21 (s, 1 H), 1.87 - 2.14 (m, 2 H), 1.13 (d, *J*=6.7 Hz, 6 H)
40	(300 MHz, $CDCl_3$) δ ppm 10.04 (s, 1H-NH), 7.87 (s, 1H), 7.39 (d, *J*=8.6 Hz, 2H), 7.01 (s, 2H), 5.14-5.02 (m, 1H), 4.11-4.00 (m, 2H), 3.95-3.83 (m, 5H), 3.70-3.51 (m, 3H), 3.32-3.25 (m, 4H), 3.13 (sept, J=6.8 Hz, 1H), 2.50-2.33 (m, 1H), 2.26-2.14 (m, 1H), 2.12-1.86 (m, 2H), s1.49 (t, J=7.5 Hz, 3H), 1.11 (d, J=6.9 Hz, 6H)
41	(300 MHz, $CDCl_3$) δ ppm 8.02 - 8.07 (m, 2 H), 8.00 (s, 1 H), 7.59 (t, *J*=7.9 Hz, 2 H), 7.34 - 7.44 (m, 3 H), 6.59 (d, *J*=8.5 Hz, 2 H), 4.09 (t, *J*=7.3 Hz, 2 H), 3.75 - 3.85 (m, 2 H), 3.45 (s, 3 H), 3.26 - 3.39 (m, 1 H), 2.45 (s, 3 H), 2.26 (s, 6 H)
42	(300 MHz $CDCl_3$) δ ppm 8.01 - 8.09 (m, 2 H), 7.99 (s, 1 H), 7.55 - 7.64 (m, 2 H), 7.36 - 7.44 (m, 3 H), 6.54 - 6.63 (m, 2 H), 4.08 (t, *J*=7.2 Hz, 2 H), 3.80 (dd, *J*=7.3, 5.6 Hz, 2 H), 3.62 (q, *J*=7.4 Hz, 2 H), 3.27 - 3.38 (m, 1 H), 2.45 (s, 3 H), 2.26 (s, 6 H), 1.50 (t, *J*=7.3 Hz, 3 H)

Cpd Number	^{1}H NMR data
43	(300 MHz, $CDCl_3$) δ ppm 10.14 (br. s, 1 H), 7.96 (s, 1 H), 7.44 (d, *J*=8.8 Hz, 2 H), 7.33 - 7.40 (m, 2 H), 7.23 - 7.26 (m, 1 H), 7.05 (d, *J*=8.8 Hz, 2 H), 6.40 - 6.47 (m, 1 H), 3.88 - 3.99 (m, 4 H), 3.71 (s, 4 H), 3.43 (s, 3 H), 3.28 - 3.36 (m, 4 H), 3.21 (quin, *J*=13.7 Hz, 1 H), 1.38 (s, 6 H), 1.20 (d, *J*=6.7 Hz, 6 H)
44	(400 MHz, $CDCl_3$) δ ppm 10.20 (br. s., 1 H), 8.34 (d, *J*=2.2 Hz, 1 H), 7.83 (s, 1 H), 7.65 (dd, *J*=8.8, 2.5 Hz, 1 H), 6.76 (d, *J*=8.7 Hz, 1 H), 4.80 - 4.94 (m, 1 H), 3.83 - 3.95 (m, 4 H), 3.58 - 3.72 (m, 4 H), 3.47 (s, 3 H), 3.14 (quin, *J*=6.8 Hz, 1 H), 2.04 - 2.19 (m, 2 H), 1.92 - 2.04 (m, 4 H), 1.75 - 1.88 (m, 1 H), 1.54 - 1.63 (m, 2 H), 1.29 - 1.47 (m, 1 H), 1.17 (d, *J*=6.7 Hz, 6 H)
45	(400 MHz, $CDCl_3$) δ ppm 10.06 (br. s, 1 H), 8.33 (d, *J*=2.4 Hz, 1 H), 7.82 (s, 1 H), 7.65 (dd, *J*=8.7, 2.6 Hz, 1 H), 6.76 (d, *J*=8.9 Hz, 1 H), 4.77 - 4.96 (m, 1 H), 3.81 - 3.96 (m, 4 H), 3.58 - 3.73 (m, 6 H), 3.14 (quin, *J*=6.8 Hz, 1 H), 2.04 - 2.19 (m, 2 H), 1.92 - 2.04 (m, 4 H), 1.76 - 1.89 (m, 1 H), 1.50 (t, *J*=7.3 Hz, 3 H), 1.23 - 1.47 (m, 3 H), 1.17 (d, *J*=6.8 Hz, 6 H)
46	(300 MHz, $CDCl_3$) δ ppm 10.16 (br. s., 1 H), 7.97 (s, 1 H), 7.34 - 7.55 (m, 5 H), 7.05 (d, *J*=8.8 Hz, 2 H), 6.58 (dt, *J*=7.0, 2.2 Hz, 1 H), 5.49 - 5.57 (m, 0.5 H), 5.33 - 5.40 (m, 0.5 H), 3.88 - 4.00 (m, 4 H), 3.54 - 3.88 (m, 4 H), 3.43 (s, 3 H), 3.28 - 3.36 (m, 4 H), 3.22 (quin, *J*=13.6 Hz, 1 H), 2.03 - 2.56 (m, 2 H), 1.21 (d, *J*=6.7 Hz, 6 H)

Cpd Number	^{1}H NMR data
47	(300 MHz, $CDCl_3$) δ ppm 10.19 (br. s, 1 H), 8.36 (d, *J*=2.3 Hz, 1 H), 7.88 (s, 1 H), 7.67 (dd, *J*=8.8, 2.6 Hz, 1 H), 6.77 (d, *J*=8.8 Hz, 1 H), 4.77 - 4.97 (m, 1 H), 3.78 - 3.98 (m, 4 H), 3.60 - 3.72 (m, 4 H), 3.48 (s, 3 H), 2.43 (s, 3 H), 1.90 - 2.20 (m, 6 H), 1.74 - 1.90 (m, 2 H), 1.19 - 1.49 (m, 2 H)
48	(300 MHz, $CDCl_3$) δ ppm 10.05 (br. s., 1 H), 8.36 (d, *J*=2.1 Hz, 1 H), 7.87 (s, 1 H), 7.67 (dd, *J*=8.8, 2.6 Hz, 1 H), 6.77 (d, *J*=8.8 Hz, 1 H), 4.80 - 4.98 (m, 1 H), 3.81 - 3.94 (m, 4 H), 3.57 - 3.74 (m, 6 H), 2.43 (s, 3 H), 1.90 - 2.18 (m, 6 H), 1.63 - 1.90 (m, 3 H), 1.51 (t, *J*=7.3 Hz, 3 H), 1.31 - 1.46 (m, 1 H)
49	(300 MHz, $CDCl_3$) δ ppm 10.17 (s, 1 H), 8.50 (s, 2 H), 7.86 (s, 1 H), 4.66 - 5.07 (m, 1 H), 3.48 (s, 3 H), 3.30 (s, 6 H), 2.48 (s, 3 H), 1.90 - 2.19 (m, 8 H), 1.74 - 1.87 (m, 1 H), 1.15 - 1.51 (m, 1 H)
50	(300 MHz, $CDCl_3$) δ ppm 10.04 (s, 1 H), 8.49 (s, 2 H), 7.85 (s, 1 H), 4.81 - 4.99 (m, 1 H), 3.66 (q, *J*=7.4 Hz, 2 H), 3.29 (s, 6 H), 2.48 (s, 3 H), 1.92 - 2.17 (m, 6 H), 1.75 - 1.91 (m, 1 H), 1.55 - 1.70 (m, 2 H), 1.51 (t, *J*=7.5 Hz, 3 H), 1.30 - 1.46 (m, 1 H)
51	(300 MHz, $CDCl_3$) δ ppm 10.20 (br. s., 1 H), 8.31 (d, *J*=2.1 Hz, 1 H), 7.83 (s, 1 H), 7.61 (dd, *J*=8.8, 2.3 Hz, 1 H), 6.63 (d, *J*=8.8 Hz, 1 H), 4.11 (dd, *J*=11.6, 4.3 Hz, 2 H), 3.62 (t, *J*=1.0 Hz, 2 H), 3.47 (s, 3 H), 3.19 (quin, *J*=6.7 Hz, 1 H), 2.99 (s, 3 H), 1.82 - 2.22 (m, 8 H), 1.47 - 1.79 (m, 7 H), 1.24 - 1.50 (m, 1 H), 1.18 (d, *J*=6.7 Hz, 6 H)

Cpd Number	^{1}H NMR data
52	(400 MHz, MeOH-d_4) δ ppm 8.49 (s, 2 H), 7.83 (s, 1 H), 5.26 (br. s., 1 H), 4.21 (br. s., 2 H), 4.06 (br. s., 3 H), 3.52 - 3.75 (m, 5 H), 2.96 - 3.16 (m, 2 H), 1.91 - 2.20 (m, 6 H), 1.75 - 1.91 (m, 1 H), 1.65 (d, *J*=13.0 Hz, 2 H), 1.26 - 1.53 (m, 8 H)
53	(400 MHz, $CDCl_3$) δ ppm 8.37 (d, *J*=2.6 Hz, 1 H), 7.94 (s, 1 H), 7.69 (dd, *J*=8.7, 2.4 Hz, 1 H), 7.52 (t, *J*=2.2 Hz, 1 H), 7.40 - 7.47 (m, 1 H), 7.33 - 7.38 (m, 1 H), 6.79 (d, *J*=8.7 Hz, 1 H), 6.75 (dd, *J*=8.0, 2.4 Hz, 1 H), 3.86 - 3.94 (m, 4 H), 3.64 - 3.71 (m, 4 H), 3.43 (s, 3 H), 3.23 (quin, *J*=6.8 Hz, 1 H), 3.09 (s, 6 H), 1.26 (d, *J*=6.8 Hz, 6 H)
54	(400 MHz, $CDCl_3$) δ ppm 10.00 (br. s., 1 H), 8.37 (d, *J*=2.6 Hz, 1 H), 7.94 (s, 1 H), 7.69 (dd, *J*=8.8, 2.5 Hz, 1 H), 7.56 (t, *J*=2.1 Hz, 1 H), 7.39 - 7.48 (m, 1 H), 7.33 - 7.39 (m, 1 H), 6.79 (d, *J*=8.7 Hz, 1 H), 6.75 (dd, *J*=8.2, 2.4 Hz, 1 H), 3.85 - 3.94 (m, 4 H), 3.65 - 3.71 (m, 4 H), 3.61 (q, *J*=7.5 Hz, 2 H), 3.22 (quin, *J*=13.6 Hz, 1 H), 3.09 (s, 6 H), 1.46 (t, *J*=7.4 Hz, 3 H), 1.26 (d, *J*=6.8 Hz, 6 H)
55	(300 MHz, $CDCl_3$) δ ppm 10.25 (s, 1 H), 8.31 (d, *J*=2.1 Hz, 1 H), 7.83 (s, 1 H), 7.60 (dd, *J*=8.8, 2.3 Hz, 1 H), 6.64 (d, *J*=8.8 Hz, 1 H), 5.43 (quin, *J*=7.3 Hz, 1 H), 3.46 (s, 3 H), 3.11 - 3.25 (m, 7 H), 2.11 - 2.29 (m, 4 H), 1.95 - 2.11 (m, 2 H), 1.73 - 1.89 (m, 2 H), 1.17 (d, *J*=6.7 Hz, 6 H)
56	(300 MHz, $CDCl_3$) δ ppm 10.12 (s, 1 H), 8.31 (d, *J*=2.1 Hz, 1 H), 7.82 (s, 1 H), 7.60 (dd, *J*=8.8, 2.3 Hz, 1 H), 6.64 (d, *J*=8.8 Hz, 1 H), 5.44 (quin, *J*=7.3 Hz, 1 H), 3.64 (q, *J*=7.4 Hz, 2 H), 3.05 - 3.35 (m, 7 H), 2.13 - 2.24 (m, 4 H), 1.98 - 2.12 (m, 2 H), 1.74 - 1.91 (m, 2 H), 1.49 (t, *J*=7.5 Hz, 3 H), 1.17 (d, *J*=6.7 Hz, 6 H)

Cpd Number	^{1}H NMR data
57	(300 MHz, $CDCl_3$) δ ppm 9.95 (br. s, 1 H), 8.46 (s, 1 H), 8.39 (d, *J*=2.3 Hz, 1 H), 8.35 (d, *J*=8.2 Hz, 1 H), 8.04 (s, 1 H), 7.61 - 7.78 (m, 3 H), 6.81 (d, *J*=8.8 Hz, 1 H), 3.84 - 3.95 (m, 4 H), 3.62 - 3.72 (m, 4 H), 3.46 (s, 3 H), 2.53 (s, 3 H)
58	(300 MHz, $CDCl_3$) δ ppm 9.82 (s, 1 H), 8.47 (s, 1 H), 8.39 (d, *J*=2.1 Hz, 1 H), 8.35 (d, *J*=7.9 Hz, 1 H), 8.03 (s, 1 H), 7.59 - 7.79 (m, 3 H), 6.81 (d, *J*=8.8 Hz, 1 H), 3.85 - 3.93 (m, 4 H), 3.57 - 3.74 (m, 6 H), 2.53 (s, 3 H), 1.49 (t, *J*=7.3 Hz, 3 H)
59	(400 MHz, $CDCl_3$) δ ppm 10.11 (br. s., 1 H), 8.52 (s, 2 H), 7.93 (s, 1 H), 7.47 - 7.55 (m, 1 H), 7.43 (t, *J*=1.0 Hz, 1 H), 7.30 - 7.38 (m, 1 H), 6.70 - 6.83 (m, 1 H), 3.90 - 4.02 (m, 4 H), 3.79 - 3.90 (m, 4 H), 3.44 (s, 3 H), 3.22 (quin, *J*=13.6 Hz, 1 H), 3.09 (s, 6 H), 1.31 (d, *J*=6.8 Hz, 6 H)
60	(400 MHz, $CDCl_3$) δ ppm 9.94 (br. s., 1 H), 8.38 (dd, *J*=2.4, 0.5 Hz, 1 H), 8.02 (s, 1 H), 7.83 - 7.98 (m, 2 H), 7.71 (dd, *J*=8.7, 2.6 Hz, 1 H), 7.34 - 7.44 (m, 1 H), 6.81 (d, *J*=8.7 Hz, 1 H), 3.85 - 3.93 (m, 4 H), 3.64 - 3.72 (m, 4 H), 3.46 (s, 3 H), 2.50 (s, 3 H)
61	(300 MHz, $CDCl_3$) δ ppm 9.81 (s, 1 H), 8.38 (d, *J*=2.6 Hz, 1 H), 8.01 (s, 1 H), 7.84 - 7.98 (m, 2 H), 7.70 (dd, *J*=8.8, 2.6 Hz, 1 H), 7.32 - 7.48 (m, 1 H), 6.80 (d, *J*=8.8 Hz, 1 H), 3.84 - 3.93 (m, 4 H), 3.57 - 3.74 (m, 6 H), 2.50 (s, 3 H), 1.49 (t, *J*=7.5 Hz, 3 H)

Cpd Number	^{1}H NMR data
62	(400 MHz, $CDCl_3$) δ ppm 9.97 (br. s., 1 H), 8.52 (s, 2 H), 7.92 (s, 1 H), 7.51 - 7.56 (m, 1 H), 7.43 (t, *J*=8.1 Hz, 1 H), 7.35 (s, 1 H), 6.75 (dd, *J*=8.2, 1.9 Hz, 1 H), 3.91 - 3.99 (m, 4 H), 3.81 - 3.90 (m, 4 H), 3.61 (q, *J*=7.4 Hz, 2 H), 3.22 (quin, *J*=6.8 Hz, 1 H), 3.09 (s, 6 H), 1.46 (t, *J*=7.4 Hz, 3 H), 1.31 (d, *J*=6.8 Hz, 6 H)
63	(400 MHz $CDCl_3$) δ ppm 10.04 (br. s., 1 H), 8.28 - 8.32 (m, 1 H), 8.07 - 8.12 (m, 2 H), 7.96 (s, 1 H), 7.51 - 7.65 (m, 3 H), 7.37 - 7.44 (m, 1 H), 6.69 (d, *J*=8.9 Hz, 1 H), 3.84 - 3.93 (m, 2 H), 3.64 - 3.78 (m, 3 H), 3.45 (s, 3 H), 3.41 (s, 3 H), 3.22 (s, 3 H), 2.38 - 2.51 (m, 2 H), 2.04 - 2.17 (m, 2 H), 1.87 - 2.00 (m, 2 H)
64	(400 MHz, $CDCl_3$) δ ppm 10.19 (br. s., 1 H), 8.25 - 8.44 (m, 1 H), 7.83 (s, 1 H), 7.65 (dd, *J*=8.6, 2.5 Hz, 1 H), 6.51 (d, *J*=8.2 Hz, 1 H), 4.81 - 4.95 (m, 1 H), 3.96 (t, *J*=13.0 Hz, 2 H), 3.72 - 3.86 (m, 3 H), 3.13 (quin, *J*=6.8 Hz, 1 H), 2.49 - 2.65 (m, 2 H), 2.06 - 2.18 (m, 2 H), 1.94 - 2.03 (m, 4 H), 1.78 - 1.90 (m, 2 H), 1.62 (s, 3 H), 1.34 - 1.47 (m, 1 H), 1.17 (d, *J*=6.8 Hz, 14 H)
65	(300 MHz, $CDCl_3$) δ ppm 10.01 (s, 1 H), 8.14 (m, *J*=2.1, 2.1 Hz, 1 H), 7.99 - 8.09 (m, 2 H), 7.42 - 7.58 (m, 3 H), 7.32 - 7.40 (m, 1 H), 7.06 (d, *J*=9.1 Hz, 2 H), 3.87 - 3.99 (m, 4 H), 3.46 (s, 3 H), 3.27 - 3.35 (m, 4 H), 2.45 (s, 3 H)
66	(300 MHz, $CDCl_3$) δ ppm 9.88 (s, 1 H), 8.14 (m, *J*=2.1, 2.1 Hz, 1 H), 7.99 - 8.10 (m, 2 H), 7.40 - 7.57 (m, 3 H), 7.36 (m, *J*=2.1, 0.9 Hz, 3 H), 7.06 (d, *J*=8.8 Hz, 1 H), 3.86 - 3.98 (m, 4 H), 3.63 (q, *J*=7.4 Hz, 2 H), 3.26 - 3.37 (m, 4 H), 2.45 (s, 3 H), 1.49 (t, *J*=7.3 Hz, 3 H)

Cpd Number	^{1}H NMR data
67	(300 MHz, $CDCl_3$) δ ppm 10.00 (br. s., 1 H), 8.04 (s, 1 H), 7.93 - 8.00 (m, 1 H), 7.83 (dt, *J*=10.3, 2.2 Hz, 1 H), 7.55 (td, *J*=8.2, 6.2 Hz, 1 H), 7.41 - 7.50 (m, 2 H), 7.01 - 7.15 (m, 3 H), 3.86 - 3.96 (m, 4 H), 3.46 (s, 3 H), 3.26 - 3.37 (m, 4 H), 2.45 (s, 3 H)
68	(300 MHz, $CDCl_3$) δ ppm 9.87 (br. s., 1 H), 8.03 (s, 1 H), 7.94 - 8.01 (m, 1 H), 7.84 (dt, *J*=10.2, 2.2 Hz, 1 H), 7.55 (td, *J*=8.3, 6.3 Hz, 1 H), 7.42 - 7.50 (m, 2 H), 7.02 - 7.13 (m, 3 H), 5.59 - 5.61 (m, 1 H), 3.87 - 3.98 (m, 4 H), 3.64 (q, *J*=7.3 Hz, 2 H), 3.27 - 3.36 (m, 4 H), 2.45 (s, 3 H), 1.49 (t, *J*=7.5 Hz, 3 H)
69	(300 MHz, $CDCl_3$) δ ppm 9.90 (s, 1 H), 8.09 - 8.17 (m, 2 H), 8.04 (s, 1 H), 7.42 - 7.51 (m, 4 H), 7.06 (d, *J*=8.8 Hz, 2 H), 3.80 - 4.08 (m, 4 H), 3.46 (s, 3 H), 3.28 - 3.37 (m, 4 H), 2.45 (s, 3 H)
70	(300 MHz, $CDCl_3$) δ ppm 9.83 (br. s., 1 H), 8.10 - 8.18 (m, 2 H), 8.03 (s, 1 H), 7.39 - 7.53 (m, 4 H), 7.06 (d, *J*=9.1 Hz, 2 H), 3.87 - 3.99 (m, 4 H), 3.64 (q, *J*=7.3 Hz, 2 H), 3.24 - 3.37 (m, 4 H), 2.45 (s, 3 H), 1.49 (t, *J*=7.3 Hz, 3 H)
71	(300 MHz, $CDCl_3$) δ ppm 10.02 (s, 1H-NH), 8.32 (d, J=2.4 Hz, 1H), 8.11-8.06 (m, 2H), 7.95 (s, 1H), 7.67-7.56 (m, 3H), 7.40 (t, *J*=7.4 Hz, 1H), 6.82 (d, J=8.7 Hz, 1H), 4.05-3.92 (m, 2H), 3.75-3.62 (m, 3H), 3.44 (s, 3H), 3.02-2.92 (m, 1H), 2.50-2.35 (m, 2H), 2.15-1.82 (m, 8H)
72	(300 MHz, $CDCl_3$) δ ppm 10.09 (s, 1 H), 8.01 (s, 1 H), 7.64 - 7.71 (m, 2 H), 7.44 - 7.52 (m, 3 H), 7.06 (d, *J*=8.8 Hz, 2 H), 6.94 (dd, *J*=8.4, 2.5 Hz, 1 H), 3.90 - 3.96 (m, 7 H), 3.45 (s, 3 H), 3.29 - 3.35 (m, 4 H), 2.45 (s, 3 H)

Cpd Number	^{1}H NMR data
73	(300 MHz, $CDCl_3$) δ ppm 9.96 (s, 1 H), 8.01 (s, 1 H), 7.70 - 7.74 (m, 1 H), 7.65 - 7.70 (m, 1 H), 7.42 - 7.54 (m, 3 H), 7.06 (d, *J*=8.8 Hz, 2 H), 6.90 - 6.99 (m, 1 H), 3.89 - 3.98 (m, 7 H), 3.62 (q, *J*=7.3 Hz, 2 H), 3.27 - 3.37 (m, 4 H), 2.45 (s, 3 H), 1.48 (t, *J*=7.5 Hz, 3 H)
74	(400 MHz, $CDCl_3$) δ ppm 10.19 - 9.91 (m, 1 H), 8.36 - 8.22 (m, 1 H), 8.09 - 8.08 (m, 1 H), 8.10 (d, *J*=1.0 Hz, 2 H), 7.96 (s, 1 H), 7.69 - 7.54 (m, 3 H), 7.46 - 7.34 (m, 1 H), 6.67 (d, *J*=1.0 Hz, 1 H), 5.07 - 4.89 (m, 1 H), 4.18 - 4.02 (m, 2 H), 3.79 - 3.69 (m, 1 H), 3.68 - 3.57 (m, 1 H), 3.45 (s, 3 H), 3.02 (s, 3 H), 2.52 - 2.35 (m, 2 H), 2.20 - 2.07 (m, 2 H), 2.01 – 1.84 (m, 3 H), 1.78 - 1.68 (m, 2 H), 1.27 (s, 2 H)
75	(400 MHz, $CDCl_3$) δ ppm 10.07 (s, 1 H), 8.07 - 8.14 (m, 2 H), 7.98 (s, 1 H), 7.56 - 7.64 (m, 2 H), 7.35 - 7.42 (m, 3 H), 6.87 (d, *J*=8.9 Hz, 2 H), 3.74 (quin, *J*=8.5 Hz, 1 H), 3.65 (s, 4 H), 3.44 (s, 3 H), 3.42 (s, 3 H), 3.12 (s, 3 H), 2.37 - 2.50 (m, 2 H), 2.06 - 2.13 (m, 2 H), 1.87 - 1.95 (m, 2 H)
76	(300 MHz, $CDCl_3$) δ ppm 10.25 (br. s., 1 H), 7.97 (s, 1 H), 7.57 - 7.64 (m, 1 H), 7.45 (d, *J*=8.8 Hz, 2 H), 7.32 - 7.41 (m, 2 H), 7.05 (d, *J*=8.8 Hz, 2 H), 6.74 (dt, *J*=7.3, 2.2 Hz, 1 H), 3.87 - 3.99 (m, 4 H), 3.59 - 3.71 (m, 4 H), 3.43 (s, 3 H), 3.38 (s, 3 H), 3.27 - 3.35 (m, 4 H), 3.21 (quin, *J*=6.7 Hz, 1 H), 3.10 (s, 3 H), 1.21 (d, *J*=6.7 Hz, 6 H)
77	(300 MHz, $CDCl_3$) δ ppm 10.10 (br. s., 1 H), 8.51 (s, 2 H), 7.92 (s, 1 H), 7.50 (t, *J*=2.2 Hz, 1 H), 7.38 - 7.46 (m, 1 H), 7.31 - 7.37 (m, 1 H), 6.70 - 6.79 (m, 1 H), 3.43 (s, 3 H), 3.32 (s, 6 H), 3.24 (quin, *J*=13.7 Hz, 1 H), 3.09 (s, 6 H), 1.30 (d, *J*=6.7 Hz, 6 H)

Cpd Number	^{1}H NMR data
78	(300 MHz, $CDCl_3$) δ ppm 9.97 (br. s., 1 H), 8.51 (s, 2 H), 7.92 (s, 1 H), 7.54 (t, *J*=2.1 Hz, 1 H), 7.39 - 7.46 (m, 1 H), 7.33 - 7.38 (m, 1 H), 6.72 - 6.78 (m, 1 H), 3.61 (q, *J*=1.0 Hz, 2 H), 3.32 (s, 6 H), 3.24 (quin, *J*=13.7 Hz, 1 H), 3.09 (s, 6 H), 1.46 (t, *J*=7.3 Hz, 3 H), 1.30 (d, *J*=6.7 Hz, 6 H)
79	(400 MHz, methanol-d_4) δ ppm 7.71 - 7.81 (m, 3 H), 7.43 - 7.51 (m, 2 H), 5.13 - 5.25 (m, 1 H), 3.41 (s, 3 H), 3.10 (quin, *J*=6.8 Hz, 1 H), 2.18 (s, 3 H), 1.91 - 2.14 (m, 5 H), 1.75 - 1.86 (m, 1 H), 1.55 - 1.70 (m, 2 H), 1.27 - 1.48 (m, 2 H), 1.10 (d, *J*=6.8 Hz, 6 H)
80	(400 MHz, $CDCl_3$) δ ppm 10.20 (s, 1 H), 7.85 (s, 1 H), 7.37 - 7.44 (m, 2 H), 7.00 - 7.07 (m, 2 H), 4.81 - 4.91 (m, 1 H), 3.51 - 3.61 (m, 2 H), 3.47 (s, 3 H), 3.23 - 3.33 (m, 2 H), 3.12 (quin, *J*=6.8 Hz, 1 H), 2.82 - 2.94 (m, 1 H), 2.06 - 2.19 (m, 5 H), 1.93 - 2.04 (m, 5 H), 1.74 - 1.88 (m, 1 H), 1.56 - 1.66 (m, 2 H), 1.32 - 1.47 (m, 1 H), 1.13 (d, *J*=6.8 Hz, 6 H)
81	(400 MHz, $CDCl_3$) δ ppm 7.93 - 8.01 (m, 1 H), 7.52 - 7.59 (m, 1 H), 7.43 (d, *J*=8.7 Hz, 2 H), 7.34 - 7.41 (m, 1 H), 7.06 (d, *J*=8.5 Hz, 2 H), 6.71 - 6.79 (m, 1 H), 3.53 - 3.64 (m, 2 H), 3.43 (s, 3 H), 3.26 - 3.36 (m, 2 H), 3.20 (quin, *J*=1.0 Hz, 1 H), 3.09 (s, 6 H), 2.85 - 2.95 (m, 1 H), 2.02 - 2.20 (m, 4 H), 1.21 (d, *J*=6.8 Hz, 6 H)
82	(400 MHz, $CDCl_3$) δ ppm 10.17 (br. s., 1 H), 7.92 - 8.02 (m, 1 H), 7.52 - 7.61 (m, 1 H), 7.34 - 7.50 (m, 4 H), 6.82 - 6.93 (m, 2 H), 6.70 - 6.79 (m, 1 H), 3.62 (s, 4 H), 3.39 - 3.48 (m, 6 H), 3.22 - 3.37 (m, 1 H), 3.00 - 3.17 (m, 9 H), 1.23 (d, *J*=6.8 Hz, 6 H)

Cpd Number	^{1}H NMR data
83	(400 MHz, CDCl3) δ ppm 8.35 (d, *J*=2.4 Hz, 1 H), 7.93 (s, 1 H), 7.68 (dd, *J*=8.8, 2.5 Hz, 1 H), 7.52 (t, *J*=2.2 Hz, 1 H), 7.38 - 7.45 (m, 1 H), 7.32 - 7.38 (m, 1 H), 6.82 (d, *J*=8.7 Hz, 1 H), 6.72 - 6.77 (m, 1 H), 3.93 - 4.02 (m, 2 H), 3.61 - 3.72 (m, 2 H), 3.43 (s, 3 H), 3.21 (quin, *J*=13.7 Hz, 1 H), 3.08 (s, 6 H), 2.93 - 3.01 (m, 1 H), 1.93 - 2.14 (m, 4 H), 1.25 (d, *J*=6.8 Hz, 6 H)
84	(400 MHz, $CDCl_3$) δ ppm 8.33 (d, *J*=2.4 Hz, 1 H), 7.94 (s, 1 H), 7.63 (dd, *J*=8.8, 2.5 Hz, 1 H), 7.53 (t, *J*=2.0 Hz, 1 H), 7.33 - 7.46 (m, 2 H), 6.71 - 6.78 (m, 1 H), 6.68 (d, *J*=8.7 Hz, 1 H), 3.82 - 3.93 (m, 2 H), 3.63 - 3.71 (m, 2 H), 3.42 (s, 3 H), 3.41 (s, 3 H), 3.27 (quin, *J*=6.8 Hz, 1 H), 3.21 (s, 3 H), 3.08 (s, 6 H), 1.26 (d, *J*=6.8 Hz, 6 H)
85	(300 MHz, $CDCl_3$) δ ppm 10.08 (br. s., 1 H), 8.35 (d, *J*=2.1 Hz, 1 H), 7.94 (s, 1 H), 7.75 (t, *J*=2.1 Hz, 1 H), 7.68 (dd, *J*=8.7, 2.5 Hz, 1 H), 7.54 - 7.61 (m, 1 H), 7.42 - 7.50 (m, 1 H), 6.89 - 6.98 (m, 1 H), 6.82 (d, *J*=8.8 Hz, 1 H), 3.87 - 4.02 (m, 6 H), 3.60 - 3.72 (m, 2 H), 3.43 (s, 3 H), 3.26 - 3.35 (m, 4 H), 3.16 - 3.26 (m, 1 H), 2.91 - 3.03 (m, 1 H), 1.92 - 2.16 (m, 4 H), 1.25 (d, *J*=6.7 Hz, 6 H)
86	(300 MHz, $CDCl_3$) δ ppm 10.10 (s, 1 H), 8.32 (d, *J*=2.1 Hz, 1 H), 7.95 (s, 1 H), 7.77 (t, *J*=2.2 Hz, 1 H), 7.63 (dd, *J*=8.8, 2.3 Hz, 1 H), 7.54 - 7.60 (m, 1 H), 7.41 - 7.50 (m, 1 H), 6.89 - 6.97 (m, 1 H), 6.68 (d, *J*=8.8 Hz, 1 H), 3.90 - 3.98 (m, 4 H), 3.83 - 3.90 (m, 2 H), 3.62 - 3.72 (m, 2 H), 3.43 (s, 3 H), 3.40 (s, 3 H), 3.24 - 3.34 (m, 5 H), 3.21 (s, 3 H), 1.25 (d, *J*=6.7 Hz, 6 H)

Cpd Number	^{1}H NMR data
87	(400 MHz, $CDCl_3$) δ ppm 10.10 (br. s., 1 H), 8.33 (d, *J*=2.2 Hz, 1 H), 7.95 (s, 1 H), 7.76 (t, *J*=2.1 Hz, 1 H), 7.65 (dd, *J*=8.8, 2.5 Hz, 1 H), 7.55 - 7.59 (m, 1 H), 7.43 - 7.49 (m, 1 H), 6.93 (dd, *J*=8.1, 2.0 Hz, 1 H), 6.66 (d, *J*=8.7 Hz, 1 H), 4.78 - 5.08 (m, 1 H), 4.12 (dd, *J*=11.4, 4.4 Hz, 2 H), 3.90 - 3.97 (m, 4 H), 3.58 - 3.69 (m, 2 H), 3.43 (s, 3 H), 3.23 - 3.35 (m, 5 H), 3.01 (s, 3 H), 1.87 - 2.02 (m, 2 H), 1.68 - 1.78 (m, 2 H), 1.26 (d, *J*=6.8 Hz, 6 H)
88	(400 MHz, $CDCl_3$) δ ppm 7.93 - 8.02 (m, 1 H), 7.79 (s, 1 H), 7.55 - 7.62 (m, 1 H), 7.43 - 7.53 (m, 1 H), 7.40 (d, *J*=7.5 Hz, 2 H), 6.92 (d, *J*=8.4 Hz, 1 H), 6.86 (d, *J*=7.9 Hz, 2 H), 3.88 - 3.98 (m, 4 H), 3.64 (s, 4 H), 3.43 (s, 3 H), 3.41 (s, 3 H), 3.23 - 3.35 (m, 5 H), 3.11 (s, 3 H), 1.23 (d, *J*=6.7 Hz, 6 H)
89	(400 MHz, $CDCl_3$) δ ppm 8.34 (d, *J*=2.2 Hz, 1 H), 7.94 (s, 1 H), 7.65 (dd, *J*=8.8, 2.5 Hz, 1 H), 7.53 (t, *J*=2.1 Hz, 1 H), 7.38 - 7.45 (m, 1 H), 7.32 - 7.38 (m, 1 H), 6.74 (dd, *J*=8.2, 1.7 Hz, 1 H), 6.66 (d, *J*=8.9 Hz, 1 H), 4.88 - 5.03 (m, 1 H), 4.12 (dd, *J*=11.4, 4.4 Hz, 2 H), 3.57 - 3.68 (m, 2 H), 3.43 (s, 3 H), 3.28 (quin, *J*=6.8 Hz, 1 H), 3.08 (s, 6 H), 3.01 (s, 3 H), 1.87 - 2.02 (m, 2 H), 1.68 - 1.78 (m, 2 H), 1.26 (d, *J*=6.7 Hz, 6 H)
90	(300 MHz, $CDCl_3$) δ ppm 10.07 (s, 1 H), 8.27 - 8.35 (m, 1 H), 7.83 (s, 0.7 H), 7.74 (s, 0.3 H), 7.57 - 7.66 (m, 1 H), 6.63 (d, *J*=8.8 Hz, 1 H), 4.79 - 5.09 (m, 2 H), 4.11 (dd, *J*=11.2, 4.4 Hz, 2 H), 3.47 - 3.70 (m, 4 H), 3.11 - 3.26 (m, 1 H), 2.99 (s, 3 H), 1.78 - 2.15 (m, 9 H), 1.61 - 1.76 (m, 4 H), 1.50 (t, *J*=7.5 Hz, 3 H), 1.35 - 1.46 (m, 1 H), 1.18 (d, *J*=6.7 Hz, 6 H)

Cpd Number	^{1}H NMR data
91	(400 MHz, $CDCl_3$) δ ppm 8.52 (s, 2 H), 7.92 (s, 1 H), 7.50 (t, *J*=2.1 Hz, 1 H), 7.39 - 7.45 (m, 1 H), 7.32 - 7.37 (m, 1 H), 6.75 (dd, *J*=8.2, 2.0 Hz, 1 H), 4.97 - 5.07 (m, 1 H), 4.13 (dd, *J*=11.4, 4.4 Hz, 2 H), 3.58 - 3.67 (m, 2 H), 3.43 (s, 3 H), 3.25 (quin, *J*=6.8 Hz, 1 H), 3.18 (s, 3 H), 3.09 (s, 6 H), 1.92 - 2.04 (m, 2 H), 1.70 - 1.78 (m, 2 H), 1.31 (d, *J*=6.8 Hz, 6 H)
92	(300 MHz, $CDCl_3$) δ ppm 8.44 - 8.55 (m, 1 H), 7.87 (s, 1 H), 7.78 (dd, *J*=8.8, 2.3 Hz, 1 H), 6.57 - 6.68 (m, 1 H), 4.75 - 4.93 (m, 1 H), 3.65 (q, *J*=7.5 Hz, 2 H), 3.19 (s, 6 H), 1.76 - 2.12 (m, 8 H), 1.55 - 1.69 (m, 3 H), 1.50 (t, *J*=7.5 Hz, 3 H), 1.00 - 1.10 (m, 2 H), 0.82 - 0.94 (m, 2 H)
93	(400 MHz, $CDCl_3$) δ ppm 10.19 (s, 1 H), 8.33 (d, *J*=1.9 Hz, 1 H), 7.83 (s, 1 H), 7.64 (dd, *J*=8.7, 2.6 Hz, 1 H), 6.76 (d, *J*=8.7 Hz, 1 H), 4.74 - 4.99 (m, 1 H), 4.05 - 4.27 (m, 2 H), 3.66 - 3.90 (m, 2 H), 3.47 (s, 3 H), 3.15 (quin, *J*=6.8 Hz, 1 H), 2.65 (dd, *J*=12.9, 10.7 Hz, 2 H), 2.04 - 2.17 (m, 2 H), 1.93 - 2.04 (m, 4 H), 1.77 - 1.87 (m, 1 H), 1.60 - 1.68 (m, 1 H), 1.35 - 1.47 (m, 1 H), 1.32 (d, *J*=6.3 Hz, 6 H), 1.21 - 1.29 (m, 1 H), 1.17 (d, *J*=6.7 Hz, 6 H)
94	(400 MHz, $CDCl_3$) δ ppm 10.19 (s, 1 H), 8.25 - 8.34 (m, 1 H), 7.83 (s, 1 H), 7.62 (dd, *J*=8.8, 2.5 Hz, 1 H), 6.73 (d, *J*=8.7 Hz, 1 H), 4.81 - 4.92 (m, 1 H), 3.87 - 3.94 (m, 2 H), 3.59 - 3.67 (m, 2 H), 3.51 (s, 2 H), 3.47 (s, 3 H), 3.16 (quin, *J*=6.8 Hz, 1 H), 2.06 - 2.20 (m, 2 H), 1.93 - 2.04 (m, 4 H), 1.78 - 1.89 (m, 1 H), 1.60 - 1.76 (m, 1 H), 1.36 - 1.50 (m, 1 H), 1.34 (s, 6 H), 1.23 - 1.27 (m, 1 H), 1.18 (d, *J*=6.7 Hz, 6 H)

Cpd Number	^{1}H NMR data
95	(400 MHz, $CDCl_3$) δ ppm 8.52 (s, 2 H), 7.92 (s, 1 H), 7.49 (t, *J*=2.2 Hz, 1 H), 7.40 - 7.46 (m, 1 H), 7.31 - 7.37 (m, 1 H), 6.76 (dd, *J*=8.4, 1.9 Hz, 1 H), 4.19 - 4.28 (m, 2 H), 3.87 - 3.96 (m, 2 H), 3.43 (s, 3 H), 3.20 (quin, *J*=6.8 Hz, 1 H), 3.09 (s, 6 H), 2.95 - 3.04 (m, 1 H), 1.92 - 2.13 (m, 4 H), 1.31 (d, *J*=6.8 Hz, 6 H)
96	(400 MHz, $CDCl_3$) δ ppm 7.96 (s, 1 H), 7.55 (t, *J*=1.8 Hz, 1 H), 7.33 - 7.46 (m, 4 H), 6.93 (d, *J*=8.9 Hz, 2 H), 6.70 - 6.76 (m, 1 H), 4.10 - 4.17 (m, 2 H), 3.92 - 4.04 (m, 1 H), 3.51 - 3.62 (m, 2 H), 3.42 (s, 3 H), 3.30 (quin, *J*=6.8 Hz, 1 H), 3.09 (s, 6 H), 2.93 (s, 3 H), 1.89 - 2.01 (m, 2 H), 1.73 - 1.82 (m, 2 H), 1.23 (d, *J*=6.8 Hz, 6 H)
97	(400 MHz, $CDCl_3$) δ ppm 10.12 (br. s., 1 H), 7.94 - 8.00 (m, 1 H), 7.78 (t, *J*=2.0 Hz, 1 H), 7.56 - 7.61 (m, 1 H), 7.46 (t, *J*=8.2 Hz, 1 H), 7.42 (d, *J*=8.5 Hz, 2 H), 6.88 - 6.99 (m, 3 H), 4.14 (dd, *J*=11.4, 4.4 Hz, 2 H), 3.96 - 4.03 (m, 1 H), 3.90 - 3.96 (m, 4 H), 3.52 - 3.62 (m, 2 H), 3.43 (s, 3 H), 3.24 - 3.37 (m, 5 H), 2.93 (s, 3 H), 1.89 - 2.04 (m, 2 H), 1.73 - 1.83 (m, 2 H), 1.23 (d, *J*=6.8 Hz, 6 H)
98	(400 MHz, $CDCl_3$) δ ppm 10.19 (s, 1 H), 8.32 (d, *J*=1.9 Hz, 1 H), 7.83 (s, 1 H), 7.64 (dd, *J*=8.8, 2.5 Hz, 1 H), 6.80 (d, *J*=8.7 Hz, 1 H), 4.82 - 4.93 (m, 1 H), 4.37 - 4.49 (m, 2 H), 3.47 (s, 3 H), 3.23 - 3.35 (m, 2 H), 3.14 (quin, *J*=6.8 Hz, 1 H), 2.03 - 2.19 (m, 4 H), 1.92 - 2.04 (m, 4 H), 1.78 - 1.89 (m, 1 H), 1.58 - 1.69 (m, 4 H), 1.48 (s, 3 H), 1.34 - 1.45 (m, 1 H), 1.17 (d, *J*=6.7 Hz, 6 H)

Cpd Number	^{1}H NMR data
99	(400 MHz, $CDCl_3$) δ ppm 8.52 (s, 2 H), 7.93 (s, 1 H), 7.73 (t, *J*=1.9 Hz, 1 H), 7.52 - 7.59 (m, 1 H), 7.43 - 7.51 (m, 1 H), 6.89 - 6.99 (m, 1 H), 4.17 - 4.29 (m, 2 H), 3.87 - 3.98 (m, 6 H), 3.44 (s, 3 H), 3.27 - 3.34 (m, 4 H), 3.21 (quin, *J*=6.8 Hz, 1 H), 2.94 - 3.05 (m, 1 H), 1.91 - 2.12 (m, 4 H), 1.31 (d, *J*=6.8 Hz, 6 H)
100	(400 MHz, $CDCl_3$) δ ppm 8.03 - 8.07 (m, 2 H), 8.01 (s, 1 H), 7.53 - 7.64 (m, 2 H), 7.44 (d, *J*=8.7 Hz, 2 H), 7.34 - 7.42 (m, 1 H), 6.69 (d, *J*=8.7 Hz, 2 H), 3.52 - 3.66 (m, 2 H), 3.37 - 3.48 (m, 4 H), 3.26 (t, *J*=8.6 Hz, 1 H), 2.86 - 2.97 (m, 1 H), 2.50 (s, 3 H), 2.36 (s, 6 H), 2.24 - 2.33 (m, 1 H), 1.92 - 2.09 (m, 1 H)
101	(400 MHz, $CDCl_3$) δ ppm 10.11 (br. s., 1 H), 7.78 - 7.87 (m, 2 H), 7.51 (s, 1 H), 7.43 (t, *J*=7.8 Hz, 1 H), 7.17 (d, *J*=7.5 Hz, 1 H), 3.50 (quin, *J*=6.8 Hz, 1 H), 3.41 (s, 3 H), 3.25 - 3.34 (m, 4 H), 2.49 (s, 3 H), 1.80 - 1.90 (m, 4 H), 1.67 - 1.77 (m, 2 H), 1.49 (d, *J*=6.8 Hz, 6 H)
102	(400 MHz, $CDCl_3$) δ ppm 7.86 (s, 1 H), 7.80 - 7.84 (m, 1 H), 7.50 (s, 1 H), 7.44 (t, *J*=7.9 Hz, 1 H), 7.13 - 7.19 (m, 1 H), 3.59 (q, *J*=7.5 Hz, 2 H), 3.50 (quin, *J*=6.8 Hz, 1 H), 3.25 - 3.34 (m, 4 H), 2.49 (s, 3 H), 1.80 - 1.90 (m, 4 H), 1.68 - 1.77 (m, 2 H), 1.49 (d, *J*=6.8 Hz, 6 H), 1.45 (t, *J*=1.0 Hz, 3 H)
103	(400 MHz, $CDCl_3$) δ ppm 10.21 (br. s., 1 H), 7.85 (s, 1 H), 7.32 - 7.53 (m, 2 H), 6.92 - 7.14 (m, 2 H), 4.79 - 4.97 (m, 1 H), 3.52 - 3.62 (m, 3 H), 3.47 (s, 3 H), 3.22 - 3.34 (m, 2 H), 2.82 - 2.94 (m, 1 H), 2.23 - 2.37 (m, 2 H), 1.91 - 2.21 (m, 12 H), 1.75 - 1.91 (m, 3 H), 1.52 - 1.70 (m, 2 H), 1.33 - 1.47 (m, 1 H)

Cpd Number	^{1}H NMR data
104	(400 MHz, $CDCl_3$) δ ppm 8.29 (d, *J*=2.2 Hz, 1 H), 7.83 (s, 1 H), 7.62 (dd, *J*=8.7, 2.4 Hz, 1 H), 6.80 (d, *J*=8.9 Hz, 1 H), 4.81 - 4.96 (m, 1 H), 3.88 - 4.03 (m, 2 H), 3.53 - 3.71 (m, 3 H), 3.47 (s, 3 H), 2.90 - 3.01 (m, 1 H), 2.24 - 2.46 (m, 2 H), 1.95 - 2.21 (m, 12 H), 1.76 - 1.95 (m, 3 H), 1.52 - 1.70 (m, 2 H), 1.32 - 1.50 (m, 1 H)
105	(300 MHz, $CDCl_3$) δ ppm 10.20 (m, 1H-NH), 7.95 (s, 1H), 7.43 (dd, J=1.8, 6.4 Hz, 2H), 7.40- 7.35 (m, 2H), 7.30-7.28 (m, 1H), 7.04 (dd, J= 2.2, 6.5 Hz, 2H), 6.48 (quint, J=3.5, 5.3 Hz, 1H), 4.87-4.79 (m, 1H), 4.31 (t, J=7.4 Hz, 2H), 3.79 (t, J=4.9 Hz, 4H), 3.81 (q, J=4.8, 8.5 Hz, 2H), 3.42 (s, 3H), 3.32-3.29 (m, 4H), 3.21 (quint, J=6.7, 13.5, 1H), 2.4 (s, 1H), 1.2 (d, J=6.7, 6H)
106	(300 MHz, $CDCl_3$) δ ppm 10.20 (s, 1 H), 8.30 (d, *J*=2.1 Hz, 1 H), 7.82 (s, 1 H), 7.59 (dd, *J*=1.0 Hz, 1 H), 6.50 (d, *J*=8.8 Hz, 1 H), 4.76 - 4.95 (m, 1 H), 4.10 - 4.23 (m, 1 H), 3.58 - 3.73 (m, 4 H), 3.47 (s, 3 H), 3.42 (s, 3 H), 3.19 (quin, *J*=6.8 Hz, 1 H), 1.92 - 2.31 (m, 8 H), 1.73 - 1.89 (m, 1 H), 1.51 - 1.69 (m, 2 H), 1.33 - 1.49 (m, 1 H), 1.18 (d, *J*=7.0 Hz, 6 H)
107	(400 MHz, methanol-d_4) δ ppm 8.12 - 8.23 (m, 2 H), 7.95 (s, 1 H), 7.80 - 7.88 (m, 2 H), 7.47 - 7.54 (m, 2 H), 6.96 (tt, *J*=9.0, 2.3 Hz, 1 H), 4.12 - 4.23 (m, 2 H), 3.99 - 4.10 (m, 1 H), 3.82 - 3.93 (m, 2 H), 3.61 (s, 3 H), 3.42 (s, 3 H), 2.19 (s, 3 H)

Cpd Number	^{1}H NMR data
108	(400 MHz, $CDCl_3$) δ ppm 8.30 (d, *J*=2.0 Hz, 1 H), 7.85 (s, 1 H), 7.62 (dd, *J*=8.8, 2.5 Hz, 1 H), 6.77 (d, *J*=8.7 Hz, 1 H), 4.88 - 4.98 (m, 0.5 H), 4.81 - 4.88 (m, 0.5 H), 4.68 - 4.76 (m, 1 H), 3.76 - 3.97 (m, 2 H), 3.56 - 3.72 (m, 2 H), 3.25 (s, 3 H), 3.12 (quin, *J*=6.8 Hz, 1 H), 1.88 - 2.16 (m, 9 H), 1.73 - 1.83 (m, 1 H), 1.62 - 1.73 (m, 1 H), 1.44 - 1.60 (m, 2 H), 1.33 - 1.43 (m, 1 H), 1.15 (d, *J*=6.8 Hz, 6 H)
109	(400 MHz, $CDCl_3$) δ ppm 10.19 (br. s., 1 H), 7.96 (s, 1 H), 7.36 - 7.47 (m, 4 H), 7.28 - 7.34 (m, 1 H), 6.85 (d, *J*=8.7 Hz, 2 H), 6.54 - 6.60 (m, 1 H), 3.64 (s, 4 H), 3.38 - 3.47 (m, 10 H), 3.30 (quin, *J*=13.7 Hz, 1 H), 3.11 (s, 3 H), 2.03 - 2.12 (m, 4 H), 1.23 (d, *J*=6.7 Hz, 6 H)
110	(400 MHz, $CDCl_3$) δ ppm 10.19 (br. s., 1 H), 7.96 (s, 1 H), 7.34 - 7.48 (m, 4 H), 7.28 - 7.34 (m, 1 H), 6.93 (d, *J*=8.7 Hz, 2 H), 6.57 (dd, *J*=8.0, 1.7 Hz, 1 H), 4.14 (dd, *J*=11.4, 4.3 Hz, 2 H), 3.92 - 4.04 (m, 1 H), 3.51 - 3.64 (m, 2 H), 3.38 - 3.47 (m, 7 H), 3.30 (quin, *J*=6.8 Hz, 1 H), 2.93 (s, 3 H), 2.04 - 2.15 (m, 4 H), 1.86 - 2.02 (m, 2 H), 1.74 - 1.83 (m, 2 H), 1.23 (d, *J*=6.8 Hz, 6 H)
111	(400 MHz, $CDCl_3$) δ ppm 10.19 (s, 1 H), 7.95 (s, 1 H), 7.43 - 7.49 (m, 1 H), 7.36 - 7.43 (m, 3 H), 7.31 - 7.36 (m, 1 H), 6.94 (d, *J*=8.7 Hz, 2 H), 6.58 (dd, *J*=8.0, 1.4 Hz, 1 H), 4.14 (dd, *J*=11.4, 4.1 Hz, 2 H), 3.90 - 4.04 (m, 1 H), 3.73 (quin, *J*=8.4 Hz, 1 H), 3.57 (t, *J*=11.2 Hz, 2 H), 3.36 - 3.48 (m, 7 H), 2.94 (s, 3 H), 2.36 - 2.51 (m, 2 H), 2.03 - 2.15 (m, 6 H), 1.83 - 2.03 (m, 4 H), 1.73 - 1.84 (m, 2 H)

Cpd Number	^{1}H NMR data
112	(300 MHz, $CDCl_3$) δ ppm 9.87 (s, 1 H), 8.52 (s, 2 H), 8.01 - 8.13 (m, 2 H), 7.94 (s, 1 H), 7.54 - 7.69 (m, 2 H), 7.34 - 7.51 (m, 1 H), 3.92 - 4.03 (m, 4 H), 3.77 - 3.92 (m, 4 H), 3.63 (q, *J*=7.5 Hz, 2 H), 3.23 (quin, *J*=6.7 Hz, 1 H), 1.48 (t, *J*=7.5 Hz, 3 H), 1.31 (d, *J*=6.7 Hz, 6 H)
113	(300 MHz, $CDCl_3$) δ ppm 9.82 (s, 1 H), 8.03 (s, 1 H), 7.83 - 7.99 (m, 2 H), 7.31 - 7.52 (m, 3 H), 7.06 (d, *J*=8.8 Hz, 2 H), 3.86 - 3.98 (m, 4 H), 3.64 (q, *J*=7.4 Hz, 2 H), 3.25 - 3.36 (m, 4 H), 2.44 (s, 3 H), 1.49 (t, *J*=7.5 Hz, 3 H)
114	(300 MHz, $CDCl_3$) δ ppm 9.89 (s, 1 H), 8.08 (d, *J*=2.1 Hz, 1 H), 8.01 (s, 1 H), 7.90 (dd, *J*=8.2, 2.1 Hz, 1 H), 7.39 - 7.51 (m, 3 H), 7.02 - 7.14 (m, 2 H), 3.93 (s, 3 H), 3.63 (q, *J*=7.4 Hz, 2 H), 2.47 (s, 3 H), 2.41 (s, 3 H), 1.49 (t, *J*=7.3 Hz, 3 H)
115	(300 MHz, $CDCl_3$) δ ppm 10.02 (s, 1 H), 7.98 (s, 1 H), 7.69 (s, 2 H), 7.43 - 7.51 (m, 2 H), 7.02 - 7.09 (m, 3 H), 3.88 - 3.97 (m, 4 H), 3.61 (q, *J*=7.3 Hz, 2 H), 3.27 - 3.36 (m, 4 H), 2.46 (m, *J*=2.1 Hz, 9 H), 1.48 (t, *J*=7.3 Hz, 3 H)
116	(300 MHz, $CDCl_3$) δ ppm 9.82 (s, 1 H), 8.03 (s, 1 H), 7.86 - 7.99 (m, 2 H), 7.32 - 7.50 (m, 3 H), 7.06 (d, *J*=8.8 Hz, 2 H), 3.87 - 3.99 (m, 4 H), 3.64 (q, *J*=7.4 Hz, 2 H), 3.26 - 3.37 (m, 4 H), 2.44 (s, 3 H), 1.49 (t, *J*=7.5 Hz, 3 H)
117	(300 MHz, $CDCl_3$) δ ppm 10.08 (br. s., 1 H), 7.78 - 7.87 (m, 2 H), 7.53 (s, 1 H), 7.44 (t, *J*=7.8 Hz, 1 H), 7.17 (d, *J*=7.6 Hz, 1 H), 3.45 - 3.67 (m, 4 H), 3.44 (s, 3 H), 3.41 (s, 3 H), 3.05 - 3.23 (m, 2 H), 2.49 (s, 3 H), 2.06 - 2.22 (m, 2 H), 1.80 - 1.96 (m, 2 H), 1.49 (d, *J*=6.7 Hz, 6 H)

Cpd Number	^{1}H NMR data
118	(300 MHz, $CDCl_3$) δ ppm 9.97 (br. s., 1 H), 7.79 - 7.88 (m, 2 H), 7.52 (s, 1 H), 7.44 (t, *J*=7.9 Hz, 1 H), 7.17 (d, *J*=7.6 Hz, 1 H), 3.45 - 3.68 (m, 6 H), 3.44 (s, 3 H), 3.04 - 3.21 (m, 2 H), 2.45 - 2.52 (m, 3 H), 2.07 - 2.22 (m, 2 H), 1.80 - 1.96 (m, 2 H), 1.40 - 1.55 (m, 9 H)
119	(400 MHz, $CDCl_3$) δ ppm 10.16 (br. s., 1 H), 8.48 (s, 2 H), 7.81 (s, 1 H), 4.78 - 4.96 (m, 1 H), 4.13 - 4.28 (m, 2 H), 3.82 - 3.96 (m, 2 H), 3.47 (s, 3 H), 3.12 (quin, *J*=6.8 Hz, 1 H), 2.90 - 3.03 (m, 1 H), 1.87 - 2.17 (m, 9 H), 1.76 - 1.87 (m, 1 H), 1.25 - 1.47 (m, 4 H), 1.22 (d, *J*=6.7 Hz, 6 H)
120	(400 MHz, $CDCl_3$) δ ppm 10.17 (br. s., 1 H), 8.47 (s, 2 H), 7.68 - 7.94 (m, 1 H), 4.80 - 4.94 (m, 1 H), 3.88 - 3.99 (m, 2 H), 3.64 - 3.74 (m, 2 H), 3.47 (s, 3 H), 3.40 (s, 3 H), 3.33 (s, 3 H), 3.15 (quin, *J*=1.0 Hz, 1 H), 2.03 - 2.20 (m, 2 H), 1.91 - 2.04 (m, 4 H), 1.76 - 1.87 (m, 1 H), 1.51 - 1.69 (m, 2 H), 1.34 - 1.47 (m, 1 H), 1.22 (d, *J*=6.7 Hz, 6 H)
121	(300 MHz, $CDCl_3$) δ ppm 10.19 (s, 1H-NH), 8.26 (d, J=2.3, 1H), 7.82 (s, 1H), 7.56 (dd, *J*=8.8, 2.5 Hz, 1H), 6.71 (d, *J*=8.9 Hz, 1H), 4.91-4.79 (m, 1H), 3.82 (t, J=5.7 Hz, 4H), 3.64 (t, J=6.0 Hz, 4H), 3.46 (s, 3H), 3.39 (s, 6H), 3.17 (pent, *J*=6.9 Hz, 1H), 2.19-1.22 (m, 10H), 1.17 (d, *J*=6.9 Hz, 6H)

Cpd Number	^{1}H NMR data
122	(300 MHz, CDCl3) δ ppm 10.20 (s, 1 H), 8.30 (d, J=2.1 Hz, 1 H), 7.83 (s, 1 H), 7.62 (dd, J=8.8, 2.6 Hz, 1 H), 6.65 (d, J=8.8 Hz, 1 H), 5.70-5.46 (m, 1 H), 5.31 (s, 4 H), 4.99 - 4.71 (m, 1 H), 4.14 (td, J=8.6, 4.5 Hz, 1 H), 3.91 (d, J=5.6 Hz, 1 H), 3.82 – 3.65 (m, 1 H), 3.54 – 3.37 (m, 2 H), 3.18 (quin, J=6.7 Hz, 1 H), 3.05 (s, 2 H), 2.48 -2.26 (m, 1 H), 2.20 -1.72 (m, 6 H), 1.69 -1.50 (m, 2 H), 1.51 – 1.21(m, 2 H), 1.18 (d, J=6.7 Hz, 6 H)
123	(400 MHz, $CDCl_3$) δ ppm 8.48 (s, 2 H), 7.81 (s, 1 H), 4.95 - 5.07 (m, 1 H), 4.81 - 4.93 (m, 1 H), 4.12 (dd, *J*=11.4, 4.4 Hz, 2 H), 3.56 - 3.67 (m, 2 H), 3.47 (s, 3 H), 3.11 - 3.22 (m, 4 H), 2.04 - 2.18 (m, 2 H), 1.90 - 2.04 (m, 6 H), 1.78 - 1.88 (m, 1 H), 1.70 - 1.77 (m, 2 H), 1.53 - 1.69 (m, 2 H), 1.35 - 1.47 (m, 1 H), 1.22 (d, *J*=6.8 Hz, 6 H)
124	(300 MHz, $CDCl_3$) δ ppm 9.96 (s, 1 H), 8.44 - 8.51 (m, 1 H), 8.32 - 8.41 (m, 2 H), 8.00 (s, 1 H), 7.59 - 7.77 (m, 3 H), 6.83 (d, *J*=8.8 Hz, 1 H), 3.91 - 4.03 (m, 2 H), 3.62 - 3.74 (m, 2 H), 3.45 (s, 3 H), 3.24 (quin, *J*=6.8 Hz, 1 H), 2.92 - 3.05 (m, 1 H), 1.92 - 2.16 (m, 4 H), 1.26 (d, *J*=6.7 Hz, 6 H)
125	(400 MHz, $CDCl_3$) δ ppm 7.97 (s, 1 H), 7.66 (t, *J*=8.0 Hz, 1 H), 7.42 (d, *J*=8.7 Hz, 2 H), 7.16 (d, *J*=7.7 Hz, 1 H), 7.04 (d, *J*=8.7 Hz, 2 H), 6.48 (d, *J*=8.4 Hz, 1 H), 3.89 - 3.97 (m, 4 H), 3.42 (s, 3 H), 3.28 - 3.35 (m, 4 H), 3.25 (s, 6 H), 3.19 (quin, *J*=13.7 Hz, 1 H), 1.19 (d, *J*=6.7 Hz, 6 H)

Cpd Number	^{1}H NMR data
126	(400 MHz, $CDCl_3$) δ ppm 9.94 (s, 1 H), 8.06 - 8.17 (m, 2 H), 8.02 (s, 1 H), 7.62 (t, *J*=8.2 Hz, 1 H), 7.44 (d, *J*=8.5 Hz, 2 H), 7.20 - 7.25 (m, 1 H), 7.06 (d, *J*=8.7 Hz, 2 H), 3.90 - 3.97 (m, 4 H), 3.45 (s, 3 H), 3.29 - 3.37 (m, 4 H), 3.23 (quin, *J*=6.8 Hz, 1 H), 1.21 (d, *J*=6.8 Hz, 6 H)
127	(400 MHz, $CDCl_3$) δ ppm 9.95 (s, 1 H), 8.01 (s, 1 H), 7.88 - 8.00 (m, 2 H), 7.33 - 7.47 (m, 3 H), 7.05 (d, *J*=8.7 Hz, 2 H), 3.88 - 3.99 (m, 4 H), 3.46 (s, 3 H), 3.29 - 3.36 (m, 4 H), 3.23 (quin, *J*=6.8 Hz, 1 H), 1.20 (d, *J*=6.7 Hz, 6 H)
128	(400 MHz, $CDCl_3$) δ ppm 10.31 (s, 1H-NH), 7.97 (s, 1H), 7.72 (t, *J*=8.1 Hz, 1H), 7.41 (d, *J*=8.5 Hz, 2H), 7.27 (m, 1H), 7.04 (d, *J*=8.7 Hz, 2H), 6.61 (d, J=8.3 Hz, 1H), 3.95-3.86 (m, 8H), 3.69-3.64 (m, 4H), 3.41 (s, 3H), 3.32-3.28 (m, 4H), 3.19 (sept, J=6.9 Hz, 1H), 3.18 (d, J=6.7, 6H)
129	(400 MHz, methanol-d_4) δ ppm 7.97 - 8.00 (m, 1 H), 7.95 (s, 1 H), 7.67 (dt, *J*=10.3, 2.1 Hz, 1 H), 6.83 - 6.89 (m, 2 H), 6.66 (dt, *J*=10.6, 2.3 Hz, 1 H), 3.96 (s, 3 H), 3.93 (s, 3 H), 3.41 (s, 3 H), 2.33 (s, 3 H)
130	(400 MHz, $CDCl_3$) δ ppm 8.03 (s, 1 H), 7.74 - 7.90 (m, 2 H), 7.42 (d, *J*=8.7 Hz, 2 H), 7.07 (d, *J*=8.9 Hz, 2 H), 6.81 (tt, *J*=8.7, 2.3 Hz, 1 H), 3.53 - 3.63 (m, 2 H), 3.47 (s, 3 H), 3.28 - 3.37 (m, 2 H), 3.21 (quin, *J*=6.8 Hz, 1 H), 2.86 - 2.95 (m, 1 H), 2.00 - 2.20 (m, 4 H), 1.20 (d, *J*=6.8 Hz, 6 H)

Cpd Number	^{1}H NMR data
131	(400 MHz, $CDCl_3$) δ ppm 10.00 (s, 1 H), 7.94 - 8.13 (m, 2 H), 7.83 - 7.91 (m, 1 H), 7.55 (td, *J*=8.2, 6.4 Hz, 1 H), 7.39 - 7.47 (m, 2 H), 7.03 - 7.13 (m, 3 H), 3.54 - 3.63 (m, 2 H), 3.46 (s, 3 H), 3.27 - 3.37 (m, 2 H), 3.21 (quin, *J*=6.7 Hz, 1 H), 2.85 - 2.95 (m, 1 H), 1.99 - 2.21 (m, 4 H), 1.20 (d, *J*=6.8 Hz, 6 H)
132	(400 MHz, $CDCl_3$) δ ppm 9.99 (br. s., 1 H), 8.49 (s, 1 H), 8.38 (d, *J*=8.2 Hz, 1 H), 8.02 (s, 1 H), 7.68 - 7.77 (m, 1 H), 7.59 - 7.65 (m, 1 H), 7.40 (d, *J*=8.7 Hz, 2 H), 6.86 (d, *J*=8.9 Hz, 2 H), 3.65 (s, 4 H), 3.45 (s, 3 H), 3.42 (s, 3 H), 3.33 (quin, *J*=6.8 Hz, 1 H), 3.11 (s, 3 H), 1.24 (d, *J*=6.8 Hz, 6 H)
133	(400 MHz, $CDCl_3$) δ ppm 9.97 (s, 1 H), 8.48 (s, 1 H), 8.37 (d, *J*=8.2 Hz, 1 H), 8.34 (d, *J*=2.2 Hz, 1 H), 8.00 (s, 1 H), 7.69 - 7.77 (m, 1 H), 7.60 - 7.69 (m, 2 H), 6.67 (d, *J*=8.9 Hz, 1 H), 4.90 - 5.02 (m, 1 H), 4.12 (dd, *J*=11.4, 4.4 Hz, 2 H), 3.58 - 3.69 (m, 2 H), 3.46 (s, 3 H), 3.30 (quin, *J*=6.8 Hz, 1 H), 3.01 (s, 3 H), 1.88 - 2.04 (m, 2 H), 1.69 - 1.79 (m, 2 H), 1.27 (d, *J*=6.8 Hz, 6 H)
134	(400 MHz, $CDCl_3$) δ ppm 8.52 (s, 2 H), 7.97 - 8.04 (m, 2 H), 7.95 (s, 1 H), 7.28 - 7.33 (m, 2 H), 4.97 - 5.07 (m, 1 H), 4.13 (dd, *J*=11.4, 4.4 Hz, 2 H), 3.57 - 3.67 (m, 2 H), 3.45 (s, 3 H), 3.26 (quin, *J*=6.8 Hz, 1 H), 3.17 (s, 3 H), 1.91 - 2.05 (m, 2 H), 1.70 - 1.78 (m, 2 H), 1.30 (d, *J*=6.8 Hz, 6 H)

Cpd Number	^{1}H NMR data
135	(300 MHz, $CDCl_3$) δ ppm 9.97 (s, 1 H), 8.48 (s, 1 H), 8.37 (d, *J*=8.2 Hz, 1 H), 8.02 (s, 1 H), 7.68 - 7.79 (m, 1 H), 7.60 - 7.68 (m, 1 H), 7.47 (d, *J*=8.5 Hz, 2 H), 7.13 - 7.23 (m, 2 H), 3.54 - 3.67 (m, 2 H), 3.45 (s, 3 H), 3.31 - 3.43 (m, 2 H), 3.20 (quin, *J*=6.8 Hz, 1 H), 2.89 - 3.02 (m, 1 H), 2.18 - 2.35 (m, 2 H), 2.02 - 2.18 (m, 2 H), 1.21 (d, *J*=7.0 Hz, 6 H)
136	(300 MHz, $CDCl_3$) δ ppm 9.99 (s, 1H-NH), 8.33 (d, J=5.6 Hz, 1H), 8.01 (s, 1H), 7.78 (d, *J*=1.4 Hz, 1H), 7.54 (dd, *J*=1.7, 5.6 Hz, 1H), 7.41 (d, *J*=8.7 Hz, 2H), 7.04 (d, J=8.7 Hz, 2H), 3.94-3.87 (m, 8H), 3.65-3.60 (m, 4H), 3.45 (s, 3H), 3.33-3.28 (m, 4H), 3.21 (sept, J=6.9 Hz, 1H), 1.18 (d, *J*=6.9 Hz, 6H)
137	(300 MHz, $CDCl_3$) δ ppm 10.03 (s, 1 H), 8.02 - 8.13 (m, 2 H), 7.92 (s, 1 H), 7.60 (t, *J*=7.9 Hz, 2 H), 7.36 - 7.47 (m, 1 H), 7.31 (d, *J*=8.5 Hz, 2 H), 7.01 (d, *J*=8.5 Hz, 2 H), 3.89 - 3.99 (m, 4 H), 3.44 (s, 3 H), 3.23 - 3.34 (m, 4 H), 2.50 - 2.68 (m, 2 H), 1.88 - 2.08 (m, 1 H), 1.61 - 1.82 (m, 3 H), 1.36 (s, 3 H)
138	(300 MHz, $CDCl_3$) δ ppm 9.90 (s, 1 H), 8.03 - 8.12 (m, 2 H), 7.91 (s, 1 H), 7.54 - 7.66 (m, 2 H), 7.35 - 7.44 (m, 1 H), 7.31 (d, *J*=8.8 Hz, 2 H), 7.01 (d, *J*=8.8 Hz, 2 H), 3.88 - 3.99 (m, 4 H), 3.62 (q, *J*=7.3 Hz, 2 H), 3.22 - 3.34 (m, 4 H), 2.51 - 2.68 (m, 2 H), 1.88 - 2.08 (m, 1 H), 1.61 - 1.83 (m, 3 H), 1.47 (t, *J*=7.3 Hz, 3 H), 1.36 (s, 3 H)
139	(300 MHz, $CDCl_3$) δ ppm 8.52 (s, 2 H), 7.95 (s, 1 H), 7.57 - 7.67 (m, 1 H), 7.08 - 7.21 (m, 2 H), 4.16 - 4.30 (m, 2 H), 3.85 - 3.99 (m, 2 H), 3.42 (s, 3 H), 3.22 (quin, *J*=6.8 Hz, 1 H), 2.94 - 3.05 (m, 1 H), 1.90 - 2.15 (m, 4 H), 1.29 (d, *J*=6.7 Hz, 6 H)

Cpd Number	^{1}H NMR data
140	(400 MHz, $CDCl_3$) δ ppm 9.96 (s, 1 H), 8.37 (d, *J*=2.2 Hz, 1 H), 7.96 (s, 1 H), 7.56 - 7.75 (m, 2 H), 7.03 - 7.22 (m, 2 H), 6.83 (d, *J*=8.7 Hz, 1 H), 3.91 - 4.04 (m, 2 H), 3.62 - 3.72 (m, 2 H), 3.42 (s, 3 H), 3.24 (quin, *J*=6.8 Hz, 1 H), 2.93 - 3.02 (m, 1 H), 1.94 - 2.15 (m, 4 H), 1.23 (d, *J*=6.7 Hz, 6 H)
141	(400 MHz, $CDCl_3$) δ ppm 9.97 (s, 1 H), 7.98 (s, 1 H), 7.56 - 7.67 (m, 1 H), 7.45 (d, *J*=8.7 Hz, 2 H), 7.02 - 7.21 (m, 4 H), 3.51 - 3.66 (m, 2 H), 3.42 (s, 3 H), 3.27 - 3.35 (m, 2 H), 3.23 (quin, *J*=6.8 Hz, 1 H), 2.84 - 2.96 (m, 1 H), 1.99 - 2.20 (m, 4 H), 1.19 (d, *J*=6.8 Hz, 6 H)
142	(400 MHz, $CDCl_3$) δ ppm 10.03 (s, 1H-NH), 8.04 (d, J=8.0 Hz, 2H), 7.56 (t, *J*=7.7 Hz, 2H), 7.46 (s, 1H), 7.36 (t, *J*=7.4 Hz, 1H), 4.00 (pent, *J*=8.6 Hz, 1H), 3.60-3.48 (3, H), 3.44 (s, 3H), 3.40 (s, 3H), 3.16-3.07 (m, 2H), 2.68-2.57 (m, 2H), 2.47-2.37 (m, 2H), 2.19-1.97 (m, 4H), 1.94-1.84 (m, 2H)
143	(400 MHz, $CDCl_3$) δ ppm 8.02 (dd, *J*=8.5, 1.0 Hz, 2 H), 7.55 - 7.63 (m, 2 H), 7.45 (s, 1 H), 7.37 - 7.43 (m, 1 H), 4.64 (quin, *J*=8.3 Hz, 1 H), 4.00 (quin, *J*=8.4 Hz, 1 H), 3.47 - 3.65 (m, 5 H), 3.45 (s, 3 H), 3.35 - 3.43 (m, 1 H), 3.10 - 3.23 (m, 3 H), 2.69 - 2.82 (m, 2 H), 2.57 - 2.69 (m, 2 H), 2.37 - 2.50 (m, 2 H), 2.02 - 2.21 (m, 4 H), 1.85 - 1.98 (m, 2 H)
144	(400 MHz, $CDCl_3$) δ ppm 10.12 (s, 1H-NH), 7.51 (s, 1H), 7.49-7.47 (m, 1H), 7.37 (t, *J*=8.0 Hz, 1H), 7.32-7.28 (m, 1H), 6.72-6.67 (m, 1H), 3.7.-3.66 (m, 2H), 3.46 (sept, J=6.7 Hz, 1H), 3.39 (s, 3H), 3.38 (s, 3H), 3.35 (d, *J*=6.3 Hz, 2H), 3.05 (s, 6H), 3.00-2.91 (m, 2H), 1.98-1.81 (m, 3H), 1.60-1.49 (m, 2H), 1.47 (d, J=6.7 Hz, 6H)

Cpd Number	^{1}H NMR data
145	(400 MHz, $CDCl_3$) δ ppm 10.16 (s, 1 H), 8.32 (d, *J*=2.2 Hz, 1 H), 7.86 (s, 1 H), 7.64 (dd, *J*=8.7, 2.2 Hz, 1 H), 6.80 (d, *J*=8.7 Hz, 1 H), 5.02 - 5.16 (m, 1 H), 4.02 - 4.12 (m, 2 H), 3.83 - 4.01 (m, 3 H), 3.52 - 3.72 (m, 3 H), 3.47 (s, 3 H), 3.13 (quin, *J*=6.8 Hz, 1 H), 2.90 - 3.01 (m, 1 H), 2.35 - 2.50 (m, 1 H), 2.15 - 2.27 (m, 1 H), 1.87 - 2.14 (m, 6 H), 1.17 (d, *J*=6.7 Hz, 6 H)
146	(400 MHz, $CDCl_3$) δ ppm 10.00 (br. s., 1 H), 8.07 (dd, *J*=8.5, 1.0 Hz, 2 H), 7.52 - 7.65 (m, 2 H), 7.47 (s, 1 H), 7.32 - 7.42 (m, 1 H), 4.01 (quin, *J*=8.4 Hz, 1 H), 3.83 - 3.91 (m, 2 H), 3.73 - 3.81 (m, 2 H), 3.48 - 3.61 (m, 3 H), 3.45 (s, 3 H), 3.26 (s, 3 H), 3.07 - 3.17 (m, 2 H), 2.56 - 2.71 (m, 2 H), 2.39 - 2.48 (m, 2 H), 2.03 - 2.21 (m, 4 H), 1.84 - 1.97 (m, 2 H)
147	(400 MHz, DMSO-d_6) δ ppm 8.34 (d, *J*=7.9 Hz, 2 H), 7.51 - 7.66 (m, 2 H), 7.31 - 7.43 (m, 1 H), 7.28 (s, 1 H), 4.00 (quin, *J*=8.2 Hz, 1 H), 3.70 - 3.84 (m, 2 H), 3.40 - 3.55 (m, 3 H), 3.32 (s, 3 H), 3.04 - 3.18 (m, 2 H), 2.77 - 2.91 (m, 2 H), 2.52 - 2.60 (m, 1 H), 2.29 - 2.48 (m, 3 H), 1.92 - 2.16 (m, 4 H), 1.63 - 1.82 (m, 2 H)
148	(400 MHz, $CDCl_3$) δ ppm 10.05 (s, 1 H), 8.06 - 8.15 (m, 2 H), 7.98 (s, 1 H), 7.56 - 7.66 (m, 2 H), 7.36 - 7.45 (m, 3 H), 7.06 (d, *J*=8.8 Hz, 2 H), 3.88 - 4.00 (m, 4 H), 3.67 (quin, *J*=8.4 Hz, 1 H), 3.45 (s, 3 H), 3.29 - 3.38 (m, 4 H), 2.32 - 2.49 (m, 2 H), 1.98 - 2.10 (m, 2 H), 1.83 - 1.97 (m, 2 H)

Cpd Number	^{1}H NMR data
149	(400 MHz, $CDCl_3$) δ ppm 7.79 - 7.88 (m, 2 H), 7.43 (t, *J*=7.9 Hz, 1 H), 7.30 (s, 1 H), 7.17 (d, *J*=7.7 Hz, 1 H), 3.78 - 3.87 (m, 3 H), 3.68 - 3.75 (m, 1 H), 3.50 (quin, *J*=13.4 Hz, 1 H), 3.40 (s, 3 H), 2.49 (s, 3 H), 2.30 - 2.41 (m, 1 H), 2.12 - 2.22 (m, 1 H), 1.52 - 1.57 (m, 2 H), 1.47 (dd, 6 H)
150	(300 MHz, $CDCl_3$) δ ppm 7.40 (s, 1 H), 4.65 - 4.84 (m, 1 H), 3.32 - 3.61 (m, 10 H), 2.99 - 3.15 (m, 2 H), 1.75 - 2.15 (m, 12 H), 1.47 - 1.67 (m, 2 H), 1.39 (d, *J*=6.7 Hz, 6 H)
151	(400 MHz, methanol-d_4) δ ppm 8.18 - 8.25 (m, 2 H), 7.59 (t, *J*=7.6 Hz, 2 H), 7.45 - 7.49 (m, 1 H), 7.36 - 7.42 (m, 1 H), 4.06 - 4.17 (m, 1 H), 3.85 - 3.94 (m, 1 H), 3.73 - 3.82 (m, 1 H), 3.53 - 3.63 (m, 2 H), 3.40 (s, 3 H), 3.10 - 3.21 (m, 2 H), 2.56 - 2.69 (m, 2 H), 2.44 - 2.56 (m, 2 H), 2.04 - 2.22 (m, 4 H), 1.79 - 1.91 (m, 2 H), 1.23 (d, *J*=5.6 Hz, 6 H)
152	(400 MHz, methanol-d_4) δ ppm 8.16 - 8.22 (m, 2 H), 7.53 - 7.60 (m, 2 H), 7.42 - 7.45 (m, 1 H), 7.33 - 7.39 (m, 1 H), 4.02 - 4.14 (m, 1 H), 3.59 - 3.68 (m, 1 H), 3.48 - 3.58 (m, 4 H), 3.38 (s, 3 H), 3.09 - 3.18 (m, 2 H), 2.53 - 2.66 (m, 2 H), 2.41 - 2.53 (m, 2 H), 2.00 - 2.21 (m, 4 H), 1.78 - 1.93 (m, 2 H), 1.63 (sxt, *J*=1.0 Hz, 2 H), 0.98 (t, *J*=7.3 Hz, 3 H)

Cpd Number	^{1}H NMR data
153	(400 MHz, $CDCl_3$) δ ppm 7.97 - 8.15 (m, 2 H), 7.53 - 7.61 (m, 2 H), 7.49 (s, 1 H), 7.34 - 7.39 (m, 1 H), 4.01 (quin, *J*=8.4 Hz, 1 H), 3.72 - 3.79 (m, 1 H), 3.59 - 3.67 (m, 1 H), 3.42 (s, 3 H), 3.34 - 3.41 (m, 4 H), 3.26 - 3.32 (m, 1 H), 2.88 - 2.98 (m, 1 H), 2.61 - 2.77 (m, 2 H), 2.51 - 2.60 (m, 1 H), 2.41 - 2.51 (m, 2 H), 2.13 - 2.25 (m, 1 H), 2.01 - 2.12 (m, 2 H), 1.83 - 2.01 (m, 3 H), 1.23 - 1.36 (m, 1 H)
154	(400 MHz, methanol-d_4) δ ppm 8.18 - 8.22 (m, 2 H), 7.53 - 7.61 (m, 2 H), 7.45 (d, *J*=1.5 Hz, 1 H), 7.33 - 7.40 (m, 1 H), 4.27 (s, 2 H), 4.06 - 4.13 (m, 1 H), 3.73 - 3.81 (m, 1 H), 3.55 - 3.62 (m, 2 H), 3.44 - 3.54 (m, 4 H), 3.38 (s, 3 H), 3.12 - 3.21 (m, 2 H), 2.55 - 2.67 (m, 2 H), 2.42 - 2.54 (m, 2 H), 1.86 - 2.24 (m, 10 H)
155	(400 MHz, methanol-d_4) δ ppm 7.71 (s, 1 H), 7.53 (s, 1 H), 7.42 (s, 1 H), 7.38 (t, J=15.2 Hz, 1 H), 6.79 (d, J=6.6 Hz, 1 H), 3.52 - 3.65 (m, 4 H), 3.49 - 3.53 (m, 0 H), 3.45 (s, 3 H), 3.37 (s, 3 H), 3.12 - 3.25 (m, 2 H), 3.01 - 3.11 (m, 6 H), 2.17 (br. s., 2 H), 1.78 - 1.93 (m, 2 H), 1.50 (d, J=6.6 Hz, 6 H)
156	(400 MHz, methanol-d_4) δ ppm 7.98 (s, 1 H), 7.93 (d, *J*=7.8 Hz, 1 H), 7.50 (s, 1 H), 7.43 (t, *J*=7.8 Hz, 1 H), 7.15 - 7.21 (m, 1 H), 3.67 - 3.76 (m, 2 H), 3.51 - 3.63 (m, 1 H), 3.34 - 3.41 (m, 9 H), 2.93 - 3.04 (m, 2 H), 2.47 (s, 3 H), 1.90 - 1.98 (m, 2 H), 1.51 - 1.64 (m, 2 H), 1.47 (d, *J*=6.8 Hz, 6 H)

Cpd Number	^{1}H NMR data
157	(400 MHz, methanol-d_4) δ ppm 7.65 - 7.72 (m, 1 H), 7.49 (s, 1 H), 7.32 - 7.39 (m, 2 H), 6.73 - 6.81 (m, 1 H), 3.59 (quin, *J*=6.8 Hz, 1 H), 3.36 (s, 3 H),3.30 - 3.33 (m, 4H), 3.05 (s, 6 H), 1.82 - 1.91 (m, 4 H), 1.69 - 1.79 (m, 2 H), 1.47 (d, *J*=6.8 Hz, 6 H)
158	(400 MHz, $CDCl_3$) δ ppm 8.33 (s, 2 H), 8.02 (s, 1 H), 7.74 (d, *J*=1.7 Hz, 1 H), 7.67 (dd, *J*=8.8, 2.5 Hz, 1 H), 7.45 - 7.51 (m, 1 H), 6.82 (d, *J*=8.7 Hz, 1 H), 3.91 - 4.02 (m, 2 H), 3.61 - 3.73 (m, 6 H), 3.45 (s, 3 H), 3.22 (quin, *J*=6.8 Hz, 1 H), 2.93 - 3.02 (m, 1 H), 1.92 - 2.16 (m, 8 H), 1.23 (d, *J*=6.8 Hz, 6 H)
159	(400 MHz, $CDCl_3$) δ ppm 7.97 (d, *J*=7.5 Hz, 2 H), 7.55 – 7.49 (m, 3 H), 7.35 (t, *J*=7.5 Hz, 1 H), 4.60 (t, *J*=7.7 Hz, 2 H), 3.99 (p, *J*=8.5 Hz, 1 H), 3.42 – 3.32 (m, 2 H), 3.22 – 3.12 (m, 5 H), 2.65 – 2.54 (m, 2 H), 2.49 (t, *J*=7.7 Hz, 2 H), 2.44 – 2.34 (m, 2 H), 2.22 – 1.96 (m, 6 H)
160	(400 MHz, $CDCl_3$) δ ppm 10.06 (m, 1H-NH), 7.54 (s, 1H), 7.46 (t, *J*=2.1 Hz, 1H), 7.38 (t, *J*=8.1 Hz, 1H), 7.29 (dd, *J*=0.8, 7.9 Hz, 1H), 6.72 (dd, *J*=2.1, 8.2 Hz, 1H), 3.57-3.51 (m, 2H), 3.43-3.36 (m, 4H), 3.25-3.21 (m, 2H), 3.06 (bs, 6H), 2.93 (sept, *J*=3.7 Hz, 1H), 2.26-2.10 (m, 4H), 1.49 (d, *J*=6.8 Hz, 6H)
161	(400 MHz, $CDCl_3$) δ ppm 7.80 - 7.72 (m, 2 H), 7.56 (s, 1 H), 7.37 - 7.29 (m, 1 H), 7.12 - 7.02 (m, 1 H), 3.68 – 3.60 (m, 2 H), 3.52 – 3.41 (m, 3 H), 3.36 (s, 3 H), 3.32 (s, 3 H), 2.98 – 2.88 (m, 2 H), 2.78 – 2.70 (m, 1 H), 2.43 (s, 3 H), 1.94 – 1.86 (m, 2 H), 1.76 – 1.60 (m, 3 H), 1.56 – 1.42 (m, 7 H).

Cpd Number	^{1}H NMR data
162	(400 MHz, $CDCl_3$) δ ppm 7.77 - 7.87 (m, 2 H), 7.55 (s, 1 H), 7.44 (t, *J*=7.3 Hz, 1 H), 7.18 (d, *J*=7.5 Hz, 1 H), 3.74 (d, *J*=11.4 Hz, 1 H), 3.35 - 3.63 (m, 10 H), 3.07 (t, *J*=11.3 Hz, 1 H), 2.95 (t, *J*=10.1 Hz, 1 H), 2.49 (s, 3 H), 2.14 - 2.25 (m, 1 H), 1.96 - 2.08 (m, 1 H), 1.73 - 1.87 (m, 1 H), 1.43 - 1.53 (m, 6 H)
163	(400 MHz, $CDCl_3$) δ ppm 9.97 (br. s., 1 H), 7.80 - 7.89 (m, 2 H), 7.54 (s, 1 H), 7.44 (t, *J*=7.8 Hz, 1 H), 7.18 (d, *J*=7.7 Hz, 1 H), 3.70 - 3.78 (m, 1 H), 3.45 - 3.64 (m, 6 H), 3.43 (s, 3 H), 3.02 - 3.12 (m, 1 H), 2.94 (dd, *J*=11.8, 8.7 Hz, 1 H), 2.49 (s, 3 H), 2.14 - 2.25 (m, 1 H), 1.96 - 2.06 (m, 1 H), 1.72 - 1.87 (m, 1 H), 1.41 - 1.52 (m, 9 H)
164	(400 MHz, $CDCl_3$) δ ppm 10.09 (br. s., 1 H), 7.76 - 7.88 (m, 2 H), 7.53 (s, 1 H), 7.44 (t, *J*=7.8 Hz, 1 H), 7.18 (d, *J*=7.5 Hz, 1 H), 4.48 (d, *J*=5.6 Hz, 1 H), 4.36 (d, *J*=5.5 Hz, 1 H), 3.74 (d, *J*=12.1 Hz, 2 H), 3.37 - 3.52 (m, 4 H), 2.93 - 3.06 (m, 2 H), 2.49 (s, 3 H), 1.91 - 2.09 (m, 3 H), 1.59 - 1.73 (m, 2 H), 1.49 (d, *J*=6.8 Hz, 6 H)
165	(400 MHz, $CDCl_3$) δ ppm 10.03 (m, 1H-NH), 7.79 (d, *J*=9.8 Hz, 2H), 7.54 (s, 1H), 7.44 (t, *J*=7.8 Hz, 1H), 7.18 (d, *J*=7.5 Hz, 1H), 3.84 (d, *J*=12.4 Hz, 2H), 3.45-3.38 (m, 4H), 3.14-3.08 (m, 1H), 3.02 (d, *J*=11.7 Hz, 2H), 2.96 (bs, 3H), 2.48 (bs, 3H), 2.37 (d, *J*=11.7 Hz, 2H), 2.23-2.13 (m, 2H), 1.50 (d, *J*=6.8 Hz, 6H)
167	(400 MHz, $CDCl_3$) δ ppm 9.98 (br. s., 1 H), 7.86 - 8.07 (m, 2 H), 7.54 (s, 1 H), 7.19 - 7.26 (m, 2 H), 3.45 - 3.62 (m, 4 H), 3.44 (s, 3 H), 3.42 (s, 3 H), 3.10 - 3.20 (m, 2 H), 2.08 - 2.20 (m, 2 H), 1.82 - 1.95 (m, 2 H), 1.47 (d, *J*=6.7 Hz, 6 H)

Cpd Number	^{1}H NMR data
168	(400 MHz, $CDCl_3$) δ ppm 10.00 (m, 1H-NH), 8.00-7.95 (m, 2H), 7.53 (bs, 1H), 7.28-7.26 (m, 1H), 7.25 (t, *J*=3.6 Hz, 1H), 3.72 (d, *J*=12.4 Hz, 2H), 3.47 (sept, *J*=6.8 Hz, 1H), 3.41 (d, *J*=6.7 Hz, 6H), 3.37 (d, *J*=6.3 Hz, 2H), 2.99 (dt, *J*=1.7, 12.1 Hz, 2H), 1.96 (d, *J*=13.2 Hz, 2H), 1.93-1.85 (m, 1H), 1.56 (dq, *J*=3.8, 12.6 Hz, 2H), 1.48 (d, *J*=6.8 Hz, 6H)
169	(400 MHz, $CDCl_3$) δ ppm 8.27 - 8.34 (m, 2 H), 8.04 (s, 1 H), 7.63 - 7.67 (m, 1 H), 7.38 - 7.46 (m, 3 H), 7.07 (d, *J*=8.7 Hz, 2 H), 3.62 - 3.69 (m, 4 H), 3.53 - 3.62 (m, 2 H), 3.46 (s, 3 H), 3.28 - 3.38 (m, 2 H), 3.20 (quin, *J*=6.8 Hz, 1 H), 2.85 - 2.96 (m, 1 H), 2.01 - 2.21 (m, 8 H), 1.19 (d, *J*=6.8 Hz, 6 H)
170	(300 MHz, $CDCl_3$) δ ppm 7.75 - 7.91 (m, 2 H), 7.48 (s, 1 H), 7.43 (t, *J*=7.9 Hz, 1 H), 7.14 - 7.19 (m, 1 H), 3.65 (s, 4 H), 3.52 (quin, *J*=6.7 Hz, 1 H), 3.41 (s, 3 H), 3.31 (s, 3 H), 3.16 (s, 3 H), 2.49 (s, 3 H), 1.47 (d, *J*=6.6 Hz, 6 H)
171	(400 MHz, $CDCl_3$) δ ppm 7.76 - 7.92 (m, 2 H), 7.43 (t, *J*=7.7 Hz, 1 H), 7.24 (s, 1 H), 7.16 (d, *J*=7.6 Hz, 1 H), 3.74 - 3.85 (m, 4 H), 3.64 - 3.74 (m, 2 H), 3.46 - 3.61 (m, 3 H), 3.40 (s, 3 H), 2.49 (s, 3 H), 2.01 (t, *J*=6.6 Hz, 2 H), 1.66 - 1.76 (m, 4 H), 1.46 (d, *J*=6.6 Hz, 6 H)
172	(400 MHz, $CDCl_3$) δ ppm 10.00 (br. s., 1 H), 7.88 - 8.08 (m, 2 H), 7.54 (s, 1 H), 7.22 - 7.26 (m, 2 H), 3.44 - 3.66 (m, 6 H), 3.42 (s, 3 H), 3.08 - 3.19 (m, 2 H), 2.05 - 2.19 (m, 2 H), 1.82 - 1.94 (m, 2 H), 1.56 - 1.67 (m, 2 H), 1.47 (d, *J*=6.8 Hz, 6 H), 1.37 - 1.46 (m, 2 H), 0.96 (t, *J*=7.3 Hz, 3 H)

Cpd Number	^{1}H NMR data
173	(300 MHz, $CDCl_3$) δ ppm 10.00 (br. s., 1 H), 7.93 - 8.01 (m, 2 H), 7.55 (s, 1 H), 7.19 - 7.32 (m, 2 H), 3.29 - 3.51 (m, 8 H), 3.27 (s, 3 H), 1.94 - 2.06 (m, 2 H), 1.71 - 1.84 (m, 2 H), 1.47 (d, *J*=6.6 Hz, 6 H), 1.29 (s, 3 H)
174	(400 MHz, methanol-d_4) δ ppm 8.31 (d, *J*=7.8 Hz, 2 H), 7.60 - 7.64 (m, 1 H), 7.48 - 7.55 (m, 2 H), 7.46 (s, 1 H), 7.27 - 7.39 (m, 3 H), 7.16 - 7.23 (m, 1 H), 4.06 - 4.19 (m, 1 H), 3.81 - 3.88 (m, 2 H), 3.64 - 3.71 (m, 2 H), 3.47 - 3.58 (m, 3 H), 3.44 (s, 3 H), 3.04 - 3.17 (m, 2 H), 2.55 - 2.69 (m, 2 H), 2.42 - 2.54 (m, 2 H), 2.01 - 2.24 (m, 4 H), 1.78 - 1.91 (m, 2 H)
175	(300 MHz, $CDCl_3$) δ ppm 10.00 (br. s., 1 H), 7.86 - 8.07 (m, 2 H), 7.54 (s, 1 H), 7.20 - 7.32 (m, 2 H), 3.44 - 3.61 (m, 4 H), 3.42 (s, 3 H), 3.29 (d, *J*=6.6 Hz, 2 H), 3.08 - 3.23 (m, 2 H), 2.04 - 2.20 (m, 2 H), 1.81 - 1.96 (m, 3 H), 1.47 (d, *J*=7.0 Hz, 6 H), 0.96 (d, *J*=6.6 Hz, 6 H)
176	(400 MHz, $CDCl_3$) δ ppm 8.03 (d, *J*=7.5 Hz, 2 H), 7.58 (t, *J*=7.9 Hz, 2 H), 7.45 (s, 1 H), 7.33 - 7.42 (m, 1 H), 4.36 (q, *J*=8.6 Hz, 2 H), 4.00 (quin, *J*=8.4 Hz, 1 H), 3.49 - 3.62 (m, 3 H), 3.45 (s, 3 H), 3.10 - 3.19 (m, 2 H), 2.57 - 2.69 (m, 2 H), 2.38 - 2.49 (m, 2 H), 2.02 - 2.21 (m, 4 H), 1.85 - 1.97 (m, 2 H)
177	(400 MHz, $CDCl_3$) δ ppm 9.98 (br. s., 1 H), 7.91 - 8.03 (m, 2 H), 7.53 (s, 2 H), 7.22 - 7.27 (m, 2 H), 4.62 (t, *J*=7.8 Hz, 2 H), 3.36 - 3.53 (m, 6 H), 3.22 - 3.35 (m, 2 H), 2.52 (t, *J*=7.8 Hz, 2 H), 2.17 - 2.29 (m, 2 H), 2.02 - 2.16 (m, 2 H), 1.47 (d, *J*=6.7 Hz, 6 H)

Cpd Number	^{1}H NMR data
178	(400 MHz, $CDCl_3$) δ ppm 9.95 (s, 1 H), 7.97 – 7.93 (m, 2 H), 7.56 (s, 1 H), 7.27 – 7.22 (m, 2 H), 5.74 (td, J = 56.0, 4.6 Hz, 1H), 3.78 – 3.70 (m, 1 H), 3.64 – 3.66 (m, 1 H), 3.49 – 3.38 (m, 4 H), 3.00 – 2.84 (m, 2 H), 2.44 – 2.30 (m, 1 H), 2.12 – 1.96 (m, 2 H), 1.92 – 1.80 (m, 1 H), 1.52 – 1.40 (m, 7 H).
179	(400 MHz, $CDCl_3$) δ ppm 7.93 - 8.01 (m, 2 H), 7.19 - 7.26 (m, 2 H), 6.94 (s, 1 H), 4.14 (d, *J*=8.2 Hz, 2 H), 4.00 (d, *J*=8.2 Hz, 2 H), 3.79 (s, 2 H), 3.69 (t, *J*=5.1 Hz, 2 H), 3.34 - 3.45 (m, 4 H), 1.88 - 1.97 (m, 2 H), 1.63 - 1.74 (m, 2 H), 1.45 (d, *J*=6.8 Hz, 6 H)
180	(400 MHz, $CDCl_3$) δ ppm 9.99 (br. s., 1 H), 7.92 - 8.01 (m, 2 H), 7.55 (s, 1 H), 7.21 - 7.26 (m, 2 H), 3.91 (t, *J*=6.7 Hz, 2 H), 3.31 - 3.57 (m, 8 H), 1.96 - 2.03 (m, 2 H), 1.78 - 1.92 (m, 6 H), 1.47 (d, *J*=6.7 Hz, 6 H)
181	(400 MHz, $CDCl_3$) δ ppm 10.04 (br. s., 1 H), 8.05 (d, *J*=7.7 Hz, 2 H), 7.57 (t, *J*=7.9 Hz, 2 H), 7.47 (s, 1 H), 7.32 - 7.42 (m, 1 H), 4.03 - 4.16 (m, 3 H), 3.43 (s, 3 H), 2.52 - 2.67 (m, 2 H), 2.40 - 2.51 (m, 2 H), 2.08 - 2.21 (m, 1 H), 1.91 - 2.08 (m, 4 H), 1.72 - 1.91 (m, 3 H), 1.13 - 1.41 (m, 5 H)
182	(400 MHz, methanol-d_4) δ ppm 8.22 (d, J=8.4 Hz, 2 H), 7.59 (t, J=10.3 Hz, 2 H), 7.46 (s, 1 H), 7.40 (t, J=7.3 Hz, 1 H), 4.13 (t, J=8.3 Hz, 2 H), 3.37 - 3.37 (m, 2 H), 2.58 - 2.70 (m, 3 H), 2.50 (d, J=8.1 Hz, 2 H), 2.01 - 2.23 (m, 2 H), 1.85 - 1.98 (m, 4 H), 1.79 (d, J=4.0 Hz, 2 H)

Cpd Number	^{1}H NMR data
183	(400 MHz, $CDCl_3$) δ ppm 10.05 (br. s., 1 H), 8.05 (d, *J*=7.7 Hz, 2 H), 7.57 (t, *J*=7.9 Hz, 2 H), 7.46 (s, 1 H), 7.33 - 7.40 (m, 1 H), 3.99 (quin, *J*=8.4 Hz, 1 H), 3.62 - 3.71 (m, 2 H), 3.51 (t, *J*=6.1 Hz, 2 H), 3.41 (s, 3 H), 3.39 (s, 3 H), 2.96 (t, *J*=11.7 Hz, 2 H), 2.57 - 2.71 (m, 2 H), 2.37 - 2.51 (m, 2 H), 2.02 - 2.17 (m, 2 H), 1.87 - 1.99 (m, 2 H), 1.63 - 1.81 (m, 3 H), 1.46 - 1.56 (m, 2 H)
184	(400 MHz, $CDCl_3$) δ ppm 8.00 - 8.14 (m, 2 H), 7.46 - 7.62 (m, 2 H), 7.30 - 7.39 (m, 1 H), 6.89 (s, 1 H), 4.18 (s, 4 H), 3.86 (quin, *J*=7.9 Hz, 1 H), 3.40 (s, 3 H), 2.53 - 2.71 (m, 2 H), 2.35 - 2.51 (m, 2 H), 1.98 - 2.17 (m, 2 H), 1.85 - 1.98 (m, 4 H), 1.66 - 1.79 (m, 4 H)
185	(400 MHz, $CDCl_3$) δ ppm 10.03 (m, 1H-NH), 8.04 (dd, *J*=1.1, 8.7 Hz, 2H), 7.56 (t, *J*=7.6 Hz, 2H), 7.46 (s, 1H), 7.35 (t, *J*=7.4 Hz, 1H), 3.98 (q, *J*=8.4 Hz, 1H), 3.69 (d, *J*=12.5 Hz, 2H), 3.40 (s, 6H), 3.37 (d, *J*=6.2 Hz, 2H), 2.95 (dt, *J*=1.8, 12.2 Hz, 2H), 2.63 (dquint, *J*=2.3, 9.2 Hz, 2H), 2.47-2.39 (m, 2H), 2.15-2.01 (m, 2H), 1.95 (d, *J*=13.2 Hz, 2H), 1.91-1.84 (m, 1H), 2.63 (dq, *J*=3.8, 12.6 Hz, 2H)
186	(400 MHz, $CDCl_3$) δ ppm 10.08 (br. s., 1 H), 8.01 - 8.08 (m, 2 H), 7.51 - 7.59 (m, 2 H), 7.31 - 7.39 (m, 1 H), 7.24 (s, 1 H), 3.84 - 4.00 (m, 3 H), 3.62 - 3.70 (m, 2 H), 3.40 (s, 3 H), 2.57 - 2.69 (m, 2 H), 2.41 - 2.53 (m, 2 H), 1.97 - 2.16 (m, 2 H), 1.67 - 1.77 (m, 2 H), 0.72 - 0.81 (m, 1 H), 0.33 (q, *J*=4.1 Hz, 1 H)
187	(300 MHz, $CDCl_3$) δ ppm 9.99 (m, 1H-NH), 7.73 (d, *J*=1.5 Hz, 1H), 7.58 (s, 1H), 7.50 (dd, *J*=1.7, 5.6 Hz, 2H), 3.89 (t, *J*=4.6 Hz, 4H), 3.60 (t, *J*=5.1 Hz, 4H), 3.58-3.45 (m, 4H), 3.42 (s, 6H), 3.19-3.11 (m, 2H), 2.16-2.09 (m, 2H), 1.93-1.82 (m, 2H), 1.46 (d, *J*=6.8 Hz, 6H)

Cpd Number	^{1}H NMR data
188	(300 MHz, $CDCl_3$) δ ppm 8.26 (d, *J*=5.9 Hz, 1 H), 7.58 (s, 1 H), 7.45 (d, *J*=1.8 Hz, 1 H), 7.31 (dd, *J*=5.6, 1.8 Hz, 1 H), 3.40 - 3.63 (m, 14 H), 3.08 - 3.21 (m, 2 H), 2.03 - 2.18 (m, 6 H), 1.81 - 1.95 (m, 2 H), 1.47 (d, *J*=6.7 Hz, 6 H)
189	(400 MHz, $CDCl_3$) δ ppm 8.29 (br. s., 2 H), 7.98 (s, 1 H), 7.59 - 7.69 (m, 1 H), 7.50 (s, 1 H), 7.39 (d, *J*=5.5 Hz, 1 H), 6.82 (d, *J*=8.9 Hz, 1 H), 3.91 - 4.05 (m, 2 H), 3.55 - 3.78 (m, 7 H), 3.46 (s, 3 H), 2.91 - 3.02 (m, 1 H), 2.32 - 2.49 (m, 2 H), 1.83 - 2.20 (m, 12 H)
190	(400 MHz, CD_3OD) δ ppm 8.23 (dd, *J*=1.2, 8.8 Hz, 2H), 7.60 (t, *J*=7.5 Hz, 2H), 7.51 (s, 1H), 7.39 (t, *J*=7.4 Hz, 2H), 4.15-4.06 (m, 1H), 3.85 (d, *J*=12.4 Hz, 2H), 3.40 (s, 3H), 3.16-3.09 (m, 2H), 3.06 (s, 3H), 2.69-2.59 (m, 2H), 2.57-2.48 (m, 2H), 2.41-2.35 (m, 2H), 2.22-2.16 (m, 1H), 2.15-2.07 (m, 3H)
191	(400 MHz, CD_3OD) δ ppm 8.23 (d, *J*=8.2 Hz, 2H), 7.60 (dt, *J*=2.0, 7.6 Hz, 2H), 7.51 (s, 1H), 7.39 (t, *J*=7.4 Hz, 1H), 4.15-4.06 (m, 1H), 3.58-3.50 (m, 2H), 3.39 (s, 3H), 3.31-3.23 (m, 3H), 3.18-3.14 (m, 1H), 2.67-2.61 (m, 2H), 2.56-2.48 (m, 2H), 2.32-2.26 (m, 2H), 2.20-2.07 (m, 4H)
192	(300 MHz, methanol-d_4) δ ppm 8.10 - 8.22 (m, 2 H), 7.47 - 7.61 (m, 2 H), 7.27 - 7.41 (m, 1 H), 6.86 (s, 1 H), 3.87 - 4.07 (m, 5 H), 3.37 (s, 3 H), 2.43 - 2.67 (m, 4 H), 1.97 - 2.17 (m, 2 H), 1.71 - 1.86 (m, 4 H), 1.41 - 1.63 (m, 6 H)

Cpd Number	^{1}H NMR data
193	(400 MHz, methanol-d_4) δ ppm 8.02 - 8.24 (m, 2 H), 7.46 - 7.60 (m, 2 H), 7.25 - 7.42 (m, 1 H), 6.81 (s, 1 H), 4.40 (t, *J*=8.6 Hz, 2 H), 4.11 (dd, *J*=8.3, 5.4 Hz, 2 H), 3.92 (quin, *J*=7.7 Hz, 1 H), 3.63 (d, *J*=6.1 Hz, 2 H), 3.41 (s, 3 H), 3.37 (s, 3 H), 2.99 - 3.12 (m, 1 H), 2.37 - 2.65 (m, 4 H), 1.96 - 2.16 (m, 2 H)
194	(400 MHz, $CDCl_3$) δ ppm 10.01 (br. s., 1 H), 8.45-8.25 (m, 1 H), 8.16-8.03 (m, 2 H), 7.96 (s, 1 H), 7.81-7.52 (m, 3 H), 7.41 (br. s., 1 H), 6.96-6.75 (m, 1 H), 4.10-3.91 (m, 2 H), 3.88-3.74 (m, 2 H), 3.74-3.58 (m, 2 H), 3.44 (br. s., 3 H), 3.32-3.09 (m, 5 H), 3.07-2.90 (m, 1 H), 2.52-2.28 (m, 2 H), 2.21-1.95 (m, 4 H)
195	(400 MHz, $CDCl_3$) δ ppm 10.00 (br. s., 1 H), 8.31 (d, *J*=2.0 Hz, 1 H), 8.04 - 8.09 (m, 2 H), 8.01 (s, 1 H), 7.57 - 7.68 (m, 3 H), 7.40 - 7.48 (m, 1 H), 6.84 (d, *J*=8.7 Hz, 1 H), 3.93 - 4.03 (m, 2 H), 3.66 - 3.76 (m, 2 H), 3.48 - 3.59 (m, 1 H), 3.45 (s, 3 H), 2.91 - 3.09 (m, 3 H), 2.60 - 2.75 (m, 2 H), 1.96 - 2.14 (m, 4 H)
196	(400 MHz, $CDCl_3$) δ ppm 10.04 (br. s., 1 H), 8.33 (d, *J*=2.2 Hz, 1 H), 8.06 - 8.13 (m, 2 H), 7.97 (s, 1 H), 7.57 - 7.69 (m, 3 H), 7.33 - 7.45 (m, 1 H), 6.83 (d, *J*=8.9 Hz, 1 H), 3.92 - 4.04 (m, 2 H), 3.53 - 3.73 (m, 3 H), 3.45 (s, 3 H), 2.93 - 3.03 (m, 1 H), 2.14 - 2.23 (m, 2 H), 1.93 - 2.13 (m, 4 H), 1.75 - 1.85 (m, 2 H), 1.11 (s, 3 H), 1.08 (s, 3 H)

Cpd Number	^{1}H NMR data
197	(400 MHz, $CDCl_3$) δ ppm 10.01 (s, 1 H), 8.31 (dd, *J*=8.5, 2.1 Hz, 1 H), 8.04 - 8.12 (m, 2 H), 7.98 (d, *J*=5.1 Hz, 1 H), 7.59 - 7.68 (m, 3 H), 7.38 - 7.47 (m, 1 H), 6.83 (d, *J*=9.0 Hz, 1 H), 5.35 - 5.43 (m, 0.25 H), 5.21 - 5.28 (m, 0.25 H), 4.98 - 5.07 (m, 0.25 H), 4.83 - 4.94 (m, 0.25 H), 3.92 - 4.04 (m, 2 H), 3.63 - 3.76 (m, 2 H), 3.46 (s, 3 H), 3.06 - 3.17 (m, 1 H), 2.93 - 3.02 (m, 1 H), 2.59 - 2.85 (m, 2 H), 2.39 - 2.59 (m, 2 H), 1.95 - 2.16 (m, 4 H)
198	(300 MHz, $CDCl_3$) δ ppm 10.04 (s, 1 H), 8.01 - 8.09 (m, 2 H), 7.52 - 7.63 (m, 2 H), 7.48 (s, 1 H), 7.31 - 7.42 (m, 1 H), 4.33 - 4.43 (m, 2 H), 3.95 - 4.16 (m, 3 H), 3.36 - 3.52 (m, 5 H), 2.36 - 2.69 (m, 4 H), 1.80 - 2.20 (m, 5 H), 1.67 - 1.78 (m, 2 H), 1.35 - 1.55 (m, 2 H)
199	(300 MHz, $CDCl_3$) δ ppm 10.01 (m, 1H-NH), 8.04 (dd, *J*=1.2, 8.8 Hz, 2H), 7.56 (t, *J*=7.5 Hz, 2H), 7.46 (s, 1H), 7.37 (tt, 1.1, 7.4 Hz, 1H), 4.82-4.77 (m, 0.5H), 4.66-4.61 (m, 0.5H), 4.56-4.46 (m, 1H), 4.45-4.37 (m, 1H), 4.14-4.03 (m, 3H), 3.51-3.42 (m, 5H), 2.64-2.53 (m, 2H), 2.51-2.41 (m, 2H), 2.23-2.10 (m, 2H), 2.07-1.97 (m, 1H), 1.89 (d, *J*=13.1 Hz, 1H), 1.70-1.59 (m, 3H)
200	(300 MHz, $CDCl_3$) δ ppm 10.02 (m, 1H-NH), 8.04 (dt, *J*=1.3, 7.4 Hz, 2H), 7.56 (tt, 2.0, 7.5 Hz, 2H), 7.48 (s, 1H), 7.37 (tt, 1.1, 8.0 Hz, 1H), 4.16 (d, 6.4 Hz, 1H), 4.12-4.03 (m, 3H), 3.52 (dt, 2.1, 12.1 Hz, 2H), 3.33 (s, 3H), 2.64-2.51 (m, 2H), 2.50-2.39 (m, 2H), 2.28-2.20 (m, 1H), 2.19-2.09 (m, 1H), 2.07-1.97 (m, 1H), 1.83 (dd, 2.0, 13.0 Hz, 2H), 1.65-1.51 (m, 4H)

Cpd Number	^{1}H NMR data
201	(300 MHz, $CDCl_3$) δ ppm 8.36 (d, *J*=5.6 Hz, 1 H), 8.30 (d, *J*=2.1 Hz, 1 H), 8.00 (s, 1 H), 7.78 (d, *J*=1.5 Hz, 1 H), 7.64 (dd, *J*=8.8, 2.3 Hz, 1 H), 7.58 (dd, *J*=5.6, 1.8 Hz, 1 H), 6.83 (d, *J*=8.8 Hz, 1 H), 3.85 - 4.04 (m, 6 H), 3.61 - 3.76 (m, 7 H), 3.46 (s, 3 H), 2.92 - 3.04 (m, 1 H), 2.33 - 2.50 (m, 2 H), 1.86 - 2.17 (m, 8 H)
202	(400 MHz, $CDCl_3$) δ ppm 10.08 (br. s., 1 H), 8.05 (d, *J*=7.5 Hz, 2 H), 7.52 - 7.61 (m, 2 H), 7.34 - 7.41 (m, 1 H), 7.23 (s, 1 H), 3.93 (quin, *J*=8.1 Hz, 1 H), 3.78 - 3.86 (m, 3 H), 3.70 (dd, *J*=10.5, 5.0 Hz, 1 H), 3.41 (s, 3 H), 2.58 - 2.71 (m, 2 H), 2.31 - 2.50 (m, 3 H), 2.00 - 2.17 (m, 3 H), 1.49 - 1.55 (m, 2 H)
203	(400 MHz, $CDCl_3$) δ ppm 10.09 (br. s., 1 H), 8.03 - 8.09 (m, 2 H), 7.55 (t, *J*=7.9 Hz, 2 H), 7.32 - 7.39 (m, 1 H), 6.94 (s, 1 H), 4.10 - 4.30 (m, 4 H), 3.86 (quin, *J*=7.9 Hz, 1 H), 3.74 (t, *J*=5.1 Hz, 2 H), 3.41 (s, 3 H), 2.56 - 2.68 (m, 2 H), 2.40 - 2.52 (m, 2 H), 2.01 - 2.12 (m, 2 H), 1.84 - 1.93 (m, 2 H), 1.70 - 1.79 (m, 2 H), 1.58 - 1.67 (m, 2 H)
204	(400 MHz, $CDCl_3$) δ ppm 8.06 (d, *J*=7.7 Hz, 2 H), 7.56 (t, *J*=7.9 Hz, 2 H), 7.32 - 7.39 (m, 1 H), 6.93 (s, 1 H), 4.10 (s, 4 H), 3.87 (quin, *J*=7.9 Hz, 1 H), 3.68 - 3.76 (m, 4 H), 3.41 (s, 3 H), 2.56 - 2.69 (m, 2 H), 2.40 - 2.51 (m, 2 H), 2.03 - 2.14 (m, 2 H), 1.91 (t, *J*=5.2 Hz, 4 H)
205	(400 MHz, methanol-d_4) δ ppm 8.15 - 8.22 (m, 2 H), 7.51 - 7.60 (m, 2 H), 7.31 - 7.44 (m, 2 H), 4.08 (quin, *J*=8.5 Hz, 1 H), 3.37 - 3.42 (m, 5 H), 3.13 (s, 2 H), 2.43 - 2.70 (m, 4 H), 1.94 - 2.21 (m, 4 H), 1.53 - 1.66 (m, 2 H), 0.40 - 0.51 (m, 4 H)

Cpd Number	^{1}H NMR data
206	(400 MHz, methanol-d_4) δ ppm 8.13 - 8.21 (m, 2 H), 7.56 (t, *J*=7.9 Hz, 2 H), 7.32 - 7.41 (m, 2 H), 4.08 (quin, *J*=8.3 Hz, 1 H), 3.62 - 3.74 (m, 4 H), 3.38 (s, 3 H), 3.26 (s, 3 H), 3.15 (s, 3 H), 2.43 - 2.65 (m, 4 H), 1.97 - 2.20 (m, 2 H)
207	(300 MHz, $CDCl_3$) δ ppm 9.86 (m, 1H-NH), 8.04 (d, *J*=7.7 Hz, 2H), 7.56 (t, *J*=7.7 Hz, 2H), 7.45 (s, 1H), 7.36 (t, *J*=7.4 Hz, 1H), 4.12-4.08 (m, 2H), 4.04-3.97 (m, 1H), 3.95-3.87 (m, 1H), 3.58-3.49 (m, 3H), 3.46-3.38 (m, 5H), 3.12 (dt, *J*=2.7, 8.8 Hz, 2H), 2.62 (dquint, *J*=2.4, 9.2 Hz, 2H), 2.46-2.38 (m, 2H), 2.17-1.99 (m, 8H), 1.93-1.85 (m, 2H)
208	(400 MHz, $CDCl_3$) δ ppm 9.91 (br. s., 1 H), 8.07 (d, *J*=7.5 Hz, 2 H), 7.60 (t, *J*=7.9 Hz, 2 H), 7.48 (s, 1 H), 7.32 - 7.44 (m, 6 H), 5.16 (s, 2 H), 4.38 (br. s., 2 H), 4.03 (quin, *J*=8.4 Hz, 1 H), 3.86 (tt, *J*=11.8, 3.6 Hz, 1 H), 3.51 - 3.64 (m, 3 H), 3.47 (s, 3 H), 3.09 - 3.22 (m, 2 H), 2.89 (br. s., 2 H), 2.58 - 2.73 (m, 2 H), 2.39 - 2.52 (m, 2 H), 2.02 - 2.26 (m, 6 H), 1.81 - 2.02 (m, 4 H)
209	(400 MHz, $CDCl_3$) δ ppm 10.00 (br. s., 1 H), 8.37-8.25 (m, 1 H), 8.16-8.04 (m, 2 H), 8.03-7.91 (m, 1 H), 7.68-7.63 (m, 2 H), 7.63-7.59 (m, 1 H), 7.47-7.35 (m, 1 H), 6.83 (d, *J* = 8.5 Hz, 1 H), 5.12-4.78 (m, 1 H), 3.97 (ddd, *J* = 13.8, 7.4, 3.7 Hz, 2 H), 3.70 (ddd, *J* = 13.6, 7.6, 3.6 Hz, 2 H), 3.45 (s, 3 H), 3.15-3.07 (m, 1 H), 3.01-2.91 (m, 1 H), 2.79-2.59 (m, 2 H), 2.58-2.46 (m, 2 H), 2.16-1.93 (m, 4 H)

Cpd Number	^{1}H NMR data
210	(400 MHz, $CDCl_3$) δ ppm 10.00 (br. s., 1 H), 8.30 (d, *J*=2.1 Hz, 1 H), 8.11-8.05 (m, 2 H), 8.02-7.96 (m, 1 H), 7.66-7.58 (m, 3 H), 7.47-7.38 (m, 1 H), 6.83 (d, *J* = 8.9 Hz, 1 H), 5.43-5.18 (m, 1 H), 3.98 (ddd, *J* = 13.6, 7.4, 3.7 Hz, 2 H), 3.82-3.64 (m, 3 H), 3.45 (s, 3 H), 2.98 (tt, *J* = 7.7, 4.0 Hz, 1 H), 2.85-2.70 (m, 2 H), 2.58-2.39 (m, 2 H), 2.15-1.93 (m, 4 H)
211	(300 MHz, $CDCl_3$) δ ppm 10.03 (m, 1H-NH), 8.03 (dt, *J*=1.3, 8.8 Hz, 2H), 7.56 (t, *J*=1.3, 8.8 Hz, 2H), 7.45 (s, 1H), 7.35 (dt, *J*=1.1, 7.4 Hz, 1H), 4.81-4.74 (m, 1H), 4.07 (quint, *J*=8.1 Hz, 1H), 3.43-3.39 (m, 1H), 3.42 (s, 3H), 3.40 (s, 3H), 2.57 (dquint, *J*=2.1, 9.2 Hz, 2H), 2.48-2.37 (m, 2H), 2.27-2.17 (m, 2H), 2.14-1.97 (m, 4H), 1.82-1.71 (m, 2H), 1.67-1.59 (m, 2H)
212	(300 MHz, $CDCl_3$) δ ppm 10.04 (m, 1H-NH), 8.04 (dt, *J*=1.2, 7.8 Hz, 2H), 7.55 (t, *J*=7.6 Hz, 2H), 7.45 (s, 1H), 7.35 (dt, *J*=1.1, 7.1 Hz, 1H), 4.78-4.73 (m, 1H), 4.09 (quint, *J*=8.3 Hz, 1H), 3.42 (s, 3H), 3.43-3.39 (m, 1H), 3.40 (s, 3H), 2.62-2.50 (m, 2H), 2.49-2.39 (m, 2H), 2.20-1.97 (m, 4H), 1.96-1.75 (m, 6H)
213	(300 MHz, $CDCl_3$) δ ppm 10.04 (s, 1 H), 8.03 (d, *J*=7.6 Hz, 2 H), 7.56 (t, *J*=7.6 Hz, 2 H), 7.45 (s, 1 H), 7.40 – 7.28 (m, 6 H), 4.57 (s, 2 H), 3.97 (p, *J*=8.4 Hz, 1 H), 3.73 – 3.63 (m, 2 H), 3.46 (d, *J*=6.0 Hz, 2 H), 3.40 (s, 3 H), 3.02 – 2.89 (m, 2 H), 2.70 – 2.55 (m, 2 H), 2.48 – 2.36 (m, 2 H), 2.14 – 1.86 (m, 5 H), 1.66 – 1.54 (m, 2H)

Cpd Number	^{1}H NMR data
214	(400 MHz, $CDCl_3$) δ ppm 7.96 (d, *J*=7.7 Hz, 2 H), 7.52 (t, *J*=7.7 Hz, 2 H), 7.34 (t, *J*=7.7 Hz, 1 H), 6.91 (s, 1 H), 4.26 (s, 4 H), 3.85 (p, *J*=8.0 Hz, 1 H), 3.22 (s, 3 H), 2.68 – 2.52 (m, 2 H), 2.48 – 2.38 (m, 2 H), 2.30 – 2.24 (m, 4 H), 2.12 – 1.88 (m, 5 H).
215	(300 MHz, CD_3OD) δ ppm 8.19 (d, *J*=8.5 Hz, 2H), 7.57 (d, *J*=7.7 Hz, 1H), 7.37 (d, *J*=7.5 Hz, 1H), 4.12-4.02 (m, 2H), 3.73 (s, 3H), 3.66-3.55 (m, 2H), 3.54-3.44 (m, 2H), 3.38 (s, 3H), 3.14-2.99 (m, 2H), 2.67-2.56 (m, 3H), 2.54-2.43 (m, 3H), 2.28-1.98 (m, 8H)
216	(400 MHz, methanol-d_4) δ ppm 8.22 (d, J=9.2 Hz, 2 H), 7.59 (t, J=8.1 Hz, 2 H), 7.45 - 7.54 (m, 1 H), 7.39 (t, J=8.1 Hz, 1 H), 4.28 (m, J=9.5 Hz, 1 H), 3.99 - 4.21 (m, 2 H), 3.54 - 3.88 (m, 4 H), 3.44 - 3.54 (m, 1 H), 3.41 (s, 3 H), 2.88 - 3.13 (m, 2 H), 2.44 - 2.77 (m, 4 H), 2.35 (m, J=5.9 Hz, 2 H), 2.18 (s, 1 H), 2.11 (s, 3 H), 2.08 (m, J=4.4 Hz, 2 H)
218	(300 MHz, $CDCl_3$) δ ppm 10.20 (m, 1H-NH), 7.39 (s, 1H), 4.74 (tt, *J*=3.8, 11.4 Hz, 1H), 3.65 (d, *J*=12.4 Hz, 2H), 3.43 (s, 3H), 3.38 (s, 3H), 3.33 (d, *J*=6.2 Hz, 2H), 2.89 (dt, *J*=1.9, 12.4 Hz, 2H), 2.11-1.76 (m, 10H), 1.62-1.42 (m, 5H), 1.39 (s, 3H), 1.37 (s, 3H), 1.33-1.25 (m, 1H)
219	(400 MHz, $CDCl_3$) δ ppm 8.04 (d, *J*=7.8 Hz, 2H), 7.56 (t, *J*=7.8 Hz, 2H), 7.46 (s, 1H), 7.36 (t, *J*=7.5 Hz, 1H), 4.64-4.60 (m, 0.5H), 4.52-4.47 (m, 0.5H), 3.98 (quint, *J*=8.3 Hz, 1H), 3.1 (t, *J*=10.8 Hz, 2H), 3.40 (s, 3H), 2.94 (q, *J*=12.2 Hz, 2H), 2.73-2.52 (m, 4H), 2.47-2.40 (m, 2H), 2.36 (s, 6H), 2.14-2.01 (m, 3H), 1.91-1.70 (m, 4H)

Cpd Number	^{1}H NMR data
220	(400 MHz, $CDCl_3$) δ ppm 8.06 (d, *J*=7.6 Hz, 2 H), 7.54 (t, *J*=7.6 Hz, 2 H), 7.48 (s, 1 H), 7.35 (t, *J*=7.6 Hz, 1 H), 4.43 (dd, J = 47.0, 5.6 Hz, 2H), 3.98 (p, *J*=8.4 Hz, 1 H), 3.74 – 3.66 (m, 2 H), 3.38 (s, 3 H), 3.00 – 2.91 (m, 2 H), 2.68 – 2.58 (m, 2 H), 2.47 – 2.37 (m, 2 H), 2.14 – 1.92 (m, 5 H), 1.72 – 1.61 (m, 2 H)
221	(400 MHz, CD_3OD) δ ppm 8.22-8.19 (m, 2H), 7.50 (s, 1H), 7.29 (t, *J*=8.6 Hz, 2H), 3.77 (d, *J*=12.1 Hz, 2H), 3.57 (quint, *J*=6.9 Hz, 1H), 3.38 (s, 3H), 3.24 (s, 3H), 2.96 (t, *J*=12.6 Hz, 2H), 1.92 (d, *J*=12.4 Hz, 2H), 1.81-1.74 (m, 1H), 1.71-1.62 (m, 2H), 1.48 (d, *J*=6.8 Hz, 6H), 1.21 (s, 6H)
222	(400 MHz, $CDCl_3$) δ ppm 10.04 (s, 1 H), 8.04(d, *J*=7.6 Hz, 2 H), 7.55 (t, *J*=7.6 Hz, 2 H), 7.46 (s, 1 H), 7.35 (t, *J*=7.6 Hz, 1 H), 3.97 (p, *J*=8.4 Hz, 1 H), 3.40 (s, 3 H), 3.31 – 3.25 (m, 4 H), 2.68 – 2.56 (m, 2 H), 2.48 – 2.38 (m, 2 H), 2.14 – 2.02 (m, 2 H), 1.74 – 1.68 (m, 4 H), 1.53 – 1.44 (m, 10 H)
227	(400 MHz, DMSO-d_6) δ ppm 11.88 (br. s, 1 H), 8.29 - 8.38 (m, 2 H), 7.53 - 7.65 (m, 2 H), 7.29 - 7.46 (m, 2 H), 4.57 - 4.68 (m, 2 H), 4.36 - 4.51 (m, 4 H), 3.98 - 4.11 (m, 1 H), 3.70 - 3.86 (m, 4 H), 3.18 (s, 3 H), 2.30 - 2.56 (m, 4 H), 1.84 - 2.14 (m, 2 H), 1.47 (s, 3 H)
228	(400 MHz, methanol-d_4) δ ppm 8.20 (d, *J*=9.5 Hz, 2 H), 7.58 (t, *J*=8.6 Hz, 2 H), 7.44 (s, 1 H), 7.38 (t, *J*=10.0 Hz, 1 H), 4.03 - 4.25 (m, 2 H), 3.65 - 3.77 (m, 1 H), 3.50 - 3.63 (m, 2 H), 3.39 (s, 3 H), 3.13 (ddd, *J*=12.6, 9.8, 2.6 Hz, 2 H), 2.55 - 2.67 (m, 2 H), 2.42 - 2.54 (m, 2 H), 1.99 - 2.21 (m, 5 H), 1.50 - 1.90 (m, 9 H)

Cpd Number	^{1}H NMR data
229	(400 MHz, methanol-d_4) δ ppm 8.20 (d, J=9.5 Hz, 2 H), 7.57 (t, J=7.6 Hz, 2 H), 7.45 (d, J=4.2 Hz, 1 H), 7.38 (dt, J=3.7, 1.5 Hz, 1 H), 4.01 - 4.19 (m, 1 H), 3.74 - 3.87 (m, 1 H), 3.45 - 3.64 (m, 3 H), 3.39 (s, 3 H), 3.07 - 3.22 (m, 2 H), 2.57 - 2.66 (m, 2 H), 2.41 - 2.56 (m, 2 H), 2.03 - 2.22 (m, 4 H), 1.91 - 2.01 (m, 2 H), 1.72 - 1.90 (m, 4 H), 1.51 - 1.67 (m, 1 H), 1.18 - 1.44 (m, 6 H)
230	(400 MHz, methanol-d_4) δ ppm 8.15 - 8.25 (m, 2 H), 7.53 - 7.62 (m, 2 H), 7.41 - 7.46 (m, 1 H), 7.37 (td, *J*=7.5, 1.0 Hz, 1 H), 4.03 - 4.15 (m, 1 H), 3.64 - 3.75 (m, 1 H), 3.51 - 3.62 (m, 2 H), 3.43 (d, *J*=6.8 Hz, 2 H), 3.39 (s, 3 H), 3.07 - 3.20 (m, 2 H), 2.54 - 2.68 (m, 2 H), 2.42 - 2.53 (m, 2 H), 2.16 (t, *J*=9.2 Hz, 3 H), 2.08 (dd, *J*=13.7, 9.8 Hz, 1 H), 1.80 - 1.92 (m, 2 H), 1.05 - 1.15 (m, 1 H), 0.53 - 0.61 (m, 2 H), 0.27 (m, *J*=5.0, 5.0, 5.0 Hz, 2 H)
237	(300 MHz, $CDCl_3$) δ ppm 10.00 (m, 1H-NH), 8.04 (dt, *J*=1.2, 7.7 Hz, 2H), 7.57 (t, *J*=7.5 Hz, 2H), 7.46 (s, 1H), 7.37 (dt, *J*=1.1, 7.7 Hz, 1H), 4.82-4.77 (m, 0.5H), 4.66-4.61 (m, 0.5H), 4.56-4.46 (m, 1H), 4.45-4.41 (m, 1H), 4.14-4.03 (m, 3H), 3.50-3.42 (m, 5H), 2.63-2.53 (m, 2H), 2.51-2.41 (m, 2H), 2.23-2.10 (m, 2H), 2.06-1.99 (m, 1H), 1.90 (d, *J*=13.4 Hz, 1H), 1.70-1.64 (m, 1H), 1.62-1.57 (m, 2H)
238	(300 MHz, $CDCl_3$) δ ppm 10.02 (s, 1 H), 8.03 (d, *J*=7.5 Hz, 2 H), 7.56 (t, *J*=7.5 Hz, 2 H), 7.45 (s, 1 H), 7.37 (t, *J*=7.5 Hz, 1 H), 4.30 – 4.20 (m, 2 H), 4.04 (p, *J*=8.5 Hz, 1 H), 3.42 (s, 3 H), 2.91 – 2.74 (m, 1 H), 2.64 – 1.92 (m, 11H), 1.88 – 1.72 (m, 1 H)

Cpd Number	^{1}H NMR data
240	(400 MHz, $CDCl_3$) δ ppm 9.94 (m, 1H-NH), 7.97-7.93 (m, 2H), 7.56 (s, 1H), 7.27-7.23 (m, 2H), 3.58-3.52 (m, 2H), 3.43-3.36 (m, 4H), 3.28-3.22 (m, 2H), 2.97-2.91 (m, 1H), 2.26-2.11 (m, 4H), 1.48 (d, *J*=6.8 Hz, 6H)
241	(300 MHz, $CDCl_3$) δ ppm 10.04 (m, 1H-NH), 8.04 (d, *J*=8.1 Hz, 2H), 7.55 (t, *J*=7.7 Hz, 2H), 7.45 (s, 1H), 7.35 (t, *J*=7.5 Hz, 1H), 3.98 (pent, *J*= Hz, 1H), 3.71 (d, *J*= Hz, 2H), 3.40 (s, 3H) , 3.39 (s, 3H) , 3.26-3.14 (m, 1H), 2.99-2.83 (m, 2H), 2.70-2.54 (m, 2H), 2.50-2.37 (m, 2H), 2.18-2.00 (m, 3H), 1.89-1.75 (m, 1H), 1.73-1.49 (m, 4H), 1.20 (d, *J*=6.3 Hz, 3H)
242	(400 MHz, $CDCl_3$) δ ppm 10.05 (br. s., 1 H), 8.06 (d, *J*=8.1 Hz, 2 H), 7.58 (t, *J*=10.0 Hz, 2 H), 7.47 (s, 1 H), 7.35 - 7.41 (m, 1 H), 3.99 (t, *J*=8.3 Hz, 1 H), 3.77 (td, *J*=6.3, 2.6 Hz, 2 H), 3.46 (s, 3 H), 3.43 (s, 3 H), 2.95 (t, *J*=12.3 Hz, 2 H), 2.59 - 2.70 (m, 2 H), 2.46 (dt, *J*=7.8, 4.2 Hz, 2 H), 1.94 - 2.18 (m, 4 H), 1.79 (dd, *J*=12.8, 3.3 Hz, 2 H), 1.58 (s, 1 H), 1.43 (s, 3 H)
243	(300 MHz, $CDCl_3$) δ ppm 10.01 (s, 1 H), 8.03 (d, *J*=7.5 Hz, 2 H), 7.56 (t, *J*=7.5 Hz, 2 H), 7.48 (s, 1 H), 7.37(t, *J*=7.5 Hz, 1 H), 4.41 (t, *J*=5.4 Hz, 2 H), 4.02 (p, *J*=8.4 Hz, 1 H), 3.42 (s, 3 H), 3.22 – 3.08 (m, 10 H), 2.65 – 2.36 (m, 4 H), 2.20 – 1.94 (m, 2 H)
244	(300 MHz, $CDCl_3$) δ ppm 10.05 (s, 1 H), 8.04 (d, *J*=7.5 Hz, 2 H), 7.56 (t, *J*=7.5 Hz, 2 H), 7.46 (s, 1 H), 7.35 (t, *J*=7.5 Hz, 1 H), 3.98 (p, *J*=8.4 Hz, 1 H), 3.76 – 3.63 (m, 4 H), 3.40 (s, 3 H), 3.02 – 2.90 (m, 2 H), 2.71 – 2.56 (m, 2 H), 2.49 – 2.36 (m, 2 H), 2.16 – 1.92 (m, 4 H), 1.88 – 1.72 (m, 1 H), 1.66 – 1.52 (m, 2H)

Cpd Number	^{1}H NMR data
245	(400 MHz, $CDCl_3/CD_3OD$) δ ppm 10.21 (s, 1H-NH), 8.13 (s, 1H), 8.05 (d, J=8.3, 2H), 7.97 (s, 1H), 7.57 (t, *J*=7.8 Hz, 2H), 7.38 (s, 1H), 7.36 (t, J=7.4, 1H), 3.96 (m, 1H), 3.94 (s, 3H), 3.69-3.61 (m, 2H), 3.39 (s, 3H), 3.36 (d, *J*=6.1 Hz, 2H), 2.97-2.85 (m, 2H), 2.67-2.55 (m, 2H), 2.46-2.36 (m, 2H), 2.14-1.98 (m, 2H), 1.97-1.80 (m, 3H), 1.62-1.48 (m, 2H)
246	(400 MHz, $CDCl_3$) δ ppm 10.03 (m, 1H-NH), 8.27 (d, *J*=2.24 Hz, 1H), 8.09 (dd, *J*=1.1, 8.7 Hz, 2H), 7.95 (s, 1H), 7.61-7.57 (m, 3H), 7.76 (d, *J*=8.8 Hz, 1H), 6.76 (d, *J*=8.8 Hz, 1H), 3.85 (t, *J*=5.9 Hz, 4H), 3.74-3.70 (m, 1H), 3.67 (t, *J*=5.7 Hz, 4H), 3.44 (s, 3H), 3.40 (s, 6H), 2.49-2.39 (m, 2H), 2.16-2.07 (m, 2H), 1.96-1.88 (m, 2H)
247	(400 MHz, $CDCl_3$) δ ppm 10.05 (m, 1H-NH), 8.06 (d, *J*=8.2 Hz, 2H), 7.58 (t, *J*=8.0 Hz, 2H), 7.50 (s, 1H), 7.38 (t, *J*=7.4 Hz, 1H), 3.99 (pent, *J*=8.3 Hz, 1H), 3.47 (s, 2H), 3.46 (s, 3H), 3.42 (s, 3H), 3.35 (s, 3H), 3.37-3.29 (m, 2H), 2.71-2.59 (m, 2H), 2.50-2.39 (m, 2H), 2.16-2.00 (m, 4H), 1.91-1.81 (m, 2H), 1.37-1.24 (m, 2H)
248	(300 MHz, $CDCl_3$) δ ppm 9.96 (m, 1H-NH), 8.29 (d, *J*=5.6 Hz, 1H), 7.73 (d, *J*=1.6 Hz, 1H), 7.56 (s, 1H), 7.49 (dd, *J*=1.6, 5.7 Hz, 1H), 3.90-3.85 (m, 4H), 3.73-3.63 (m, 2H), 3.62-3.56 (m, 4H), 3.49-3.39 (m, 1H), 3.41 (s, 3H), 3.38 (s, 3H), 3.34 (d, *J*=6.1 Hz, 2H), 3.04-2.90 (m, 2H), 2.00-1.78 (m, 3H), 1.62-1.44 (m, 2H), 1.45 (d, *J*=6.7 Hz, 6H)

Cpd Number	^{1}H NMR data
249	(300 MHz, $CDCl_3$) δ ppm 9.93 (m, 1H-NH), 8.29 (d, *J*=5.6 Hz, 1H), 7.79 (d, *J*=1.5 Hz, 1H), 7.56 (s, 1H), 7.51 (dd, *J*=1.8, 5.6 Hz, 1H), 3.93-3.83 (m, 6H), 3.80-3.74 (m, 2H), 3.73-3.63 (m, 2H), 3.62-3.57 (m, 4H), 3.51-3.37 (m, 1H), 3.38 (s, 3H), 3.34 (d, *J*=6.1, 2H), 3.25 (s, 3H), 3.04-2.91 (m, 2H), 2.00-1.79 (m, 3H), 1.61-1.49 (m, 2H), 1.46 (d, *J*=6.9 Hz, 6H)
250	(400 MHz, $CDCl_3$) δ ppm 10.30 (s, 1 H), 8.19-8.04 (2d, *J*=8.2 Hz, 2 H), 7.77 (s, 1 H), 7.60-7.49 (m, 2 H), 7.53 and 7.38 (2s, 1 H), 7.40-7.29 (m, 1 H), 4.06-3.92 (m, 1 H), 3.64 (s, 3 H),3.70-3.60 (m, 2 H), 3.40 (s, 3 H), 3.40-3.35 (m, 2 H), 2.95-2.85 (m, 2 H), 2.70-2.57 (m, 2 H), 2.49-2.38 (m, 2 H), 2.37 (s, 3 H), 2.14-2.02 (m, 2 H), 1.99-1.80 (m, 3 H), 1.63-1.49 (m, 2 H)
251	(400 MHz, $CDCl_3$) δ ppm 10.12 (m, 1H-NH), 7.37 (s, 1H), 4.80-4.69 (m, 1H), 3.88 (t, *J*=5.6 Hz, 2H), 3.80 (t, J=5.4 Hz, 2H), 3.67-3.60 (m, 2H), 3.40-3.27 (m, 1H), 3.35 (s, 3H), 3.31 (d, *J*=6.2 Hz, 2H), 3.30 (s, 3H), 2.92-2.81 (m, 2H), 2.10-1.96 (m, 2H), 1.95-1.71 (m, 8H), 1.61-1.26 (m, 5H), 1.36 (d, *J*=6.8 Hz, 6H)
252	(400 MHz, $CDCl_3$) δ ppm 9.99 (br. s, 1 H), 8.35 (d, J=5.6 Hz, 1 H), 8.30 (d, J=2.2 Hz, 1 H), 8.01 (s, 1 H), 7.78 (d, J=1.5 Hz, 1 H), 7.59 - 7.64 (m, 1 H), 7.52 - 7.58 (m, 1 H), 6.74 - 6.82 (m, 1 H), 3.90 - 3.96 (m, 4 H), 3.80 - 3.88 (m, 4 H), 3.60 - 3.71 (m, 8 H), 3.47 (s, 3 H), 3.41 (s, 6 H), 3.17 - 3.34 (m, 1 H), 1.26 (d, J=6.8 Hz, 6 H)

Cpd Number	^{1}H NMR data
253	(400 MHz, $CDCl_3$) δ ppm 10.35 (s, 1 H), 8.24 (s, 1 H), 8.20-8.05 (2d, J=8.7 Hz, 2 H), 7.82 (m, 1 H), 7.62-7.51 (m, 2 H), 7.52 and 7.39 (2s, 1 H), 7.41-7.30 (m, 1 H), 5.92 (m, 1 H), 4.07-3.92 (m, 1 H), 3.71-3.63 (m, 2 H), 3.42 and 3.41 (2s, 3 H), 3.43-3.36 (m, 2 H), 2.98-2.88 (m, 2 H), 2.70-2.57 (m, 2 H), 2.49-2.35 (m, 2 H), 2.17-2.01 (m, 2 H), 2.00-1.82 (m, 3 H), 1.64-1.50 (m, 2 H)
254	(400 MHz, $CDCl_3$) δ ppm 10.04 (s, 1 H), 8.11 -8.00 (m, 2 H), 7.62 -7.48 (m, 3 H), 7.41-7.32 (m, 1 H), 4.71 (d, *J*=6.1 Hz, 2 H), 4.58 (d, *J*=6.1 Hz, 2 H), 4.38 (s, 2 H), 4.07 (td, *J*=8.4, 0.8 Hz, 1 H), 3.44 (s, 3 H), 2.65 -2.51 (m, 2 H), 2.50-2.34 (m, 2 H), 1.95 - 2.20 (m, 2 H), 1.57 (s, 3 H)
255	(400 MHz, $CDCl_3$) δ ppm 10.03 (s, 1 H), 8.04 (d, J=8.2 Hz, 2 H), 7.56 (t, J=8.0 Hz, 2 H), 7.49 (s, 1 H), 7.37 (t, J=7.9 Hz, 1 H), 3.96 (pent, J=8.4 Hz, 1 H), 3.45-3.38 (m, 2 H), 3.41 (s, 3 H), 3.34-3.39 (m, 2 H), 3.26 (s, 3 H), 3.23-3.18 (m, 4 H), 3.11-3.06 (m, 4 H), 2.70-2.58 (m, 4 H), 2.48-2.38 (m, 2 H), 2.12-2.02 (m, 4 H), 1.83-1.74 (m, 2 H)
256	(400 MHz, $CDCl_3$) δ ppm 10.00 (s, 1H-NH), 8.07 (d, J=8.0 Hz, 2H), 7.55 (t, *J*=8.0 Hz, 2H), 7.45 (s, 1H), 7.35 (t, *J*=7.7 Hz, 1H), 3.98 (pent, *J*=8.6 Hz, 1H), 3.86 (t, J=5.2 Hz, 2H), 3.77 (t, J=5.6 Hz, 2H), 3.72-3.63 (m, 2H), 3.40 (s, 3H), 3.37 (d, *J*=6.3 Hz, 2H), 3.25 (s, 3H), 2.99-2.90 (m, 2H), 2.68-2.56 (m, 2H), 2.47-2.37 (m, 2H), 2.16-2.00 (m, 2H), 1.99-1.81 (m, 3H), 1.63-1.50 (m, 2H)

Cpd Number	^{1}H NMR data
257	(400 MHz, $CDCl_3$) δ ppm 10.01 (br. s., 1 H), 8.27 - 8.36 (m, 1 H), 8.10 (d, *J* = 7.1 Hz, 2 H), 7.99-7.92 (m, 1 H), 7.67-7.55 (m, 3 H), 7.44-7.36 (m, 1 H), 6.87-6.75 (m, 1 H), 4.05-3.92 - (m, 2 H), 3.81-3.62 (m, 3 H), 3.45 (s, 3 H), 3.07-2.91 (m, 1 H), 2.58-2.36 (m, 2 H), 2.14-1.94 (m, 5 H), 1.81-1.69 (m, 2 H), 1.17-1.00 (m, 3 H)
258	(400 MHz, DMSO-d_6) δ ppm 8.54 (d, J=2.0 Hz, 1H), 8.36 (d, J=7.9 Hz, 2H), 7.96 (dd, J=2.0, 8.8 Hz, 1H), 7.82 (s, 1H), 7.53 (t, J=7.7 Hz, 2H), 7.25 (t, J=7.3 Hz, 1H), 7.01 (d, J=9.0 Hz, 1H), 5.22-5.03 (m, 1H), 3.98-3.89 (m, 2H), 3.55-3.44 (m, 5H), 3.18-3.14 (m, 1H), 2.91 (s, 5H), 2.68-2.59 (m, 1H), 2.08-1.93 (m, 4H), 1.81-1.63 (m, 4H)
259	(400 MHz, $CDCl_3$) δ ppm 10.01 (br. s., 1 H), 8.61 (br. s., 1 H), 8.06-7.97 (m, 3 H), 7.91 (d, *J* = 7.3 Hz, 1 H), 7.56 (t, *J* = 7.8 Hz, 1 H), 7.39-7.30 (m, 1 H), 6.87-6.80 (m, 1 H), 6.77 (d, *J* = 8.8 Hz, 1 H), 5.29 (br. s., 1 H), 4.09-3.89 (m, 2 H), 3.82-3.61 (m, 2 H), 3.55-3.40 (m, 2 H), 3.37-3.28 (m, 1 H), 3.18-3.06 (m, 1 H), 3.04-2.88 (m, 1 H), 2.18 (s, 3 H), 2.13-1.84 (m, 8 H), 1.56-1.39 (m, 9 H)
260	(400 MHz, $CDCl_3$) δ ppm 10.08 (m, 1H-NH), 8.24 (d, *J*=1.2 Hz, 1H), 8.21 (d, *J*=1.0 Hz, 1H), 7.72-7.67 (m, 2H), 7.64-7.58 (m, 4H), 7.40-7.35 (m, 1H), 7.34 (s, 1H), 4.22-4.19 (m, 2H), 3.99-3.92 (m, 2H), 3.62 (d, *J*=12.4 Hz, 2H), 3.40 (s, 3H), 3.38 (d, *J*=6.3 Hz, 2H), 2.90 (dt, *J*=1.6, 11.9 Hz, 2H), 2.69-2.59 (m, 2H), 2.48-2.40 (m, 2H), 2.14-2.04 (m, 2H), 1.95 (d, *J*=13.1 Hz, 2H), 1.90-1.82 (m, 1H), 1.61-1.50 (m, 3H)

Cpd Number	^{1}H NMR data
261	(400 MHz, $CDCl_3$) δ ppm 8.58 (t, J=6.2 Hz, 1H), 8.19 (dd, J=1.2, 6.3 Hz, 2H), 7.53 (t, J=7.5 Hz, 2H), 7.44 (s, 1H), 7.29 (tt, J=1.0, 7.4 Hz, 1H), 5.04 (s, 2H), 4.02-3.93 (m, 3H), 3.64 (d, J=12.4 Hz, 2H), 3.42-3.39 (m, 5H), 3.36 (d, J=6.3 Hz, 2H), 2.89 (dt, J=1.9, 12.3 Hz, 2H), 2.45-2.37 (m, 2H), 2.11-2.01 (m, 2H), 1.93 (d, J=13.0 Hz, 2H), 1.89-1.83 (m, 1H), 1.55 (dq, J=3.9, 12.6 Hz, 2H (2 NH. NH_2 : missing)
263	(300 MHz, $CDCl_3$) δ ppm 9.93 (m, 1H-NH), 7.38 (s, 1H), 4.43 (d, *J*=7.1 Hz, 2H), 3.84 (dd, *J*=3.4, 6.9 Hz, 4H), 3.66 (d, *J*=12.2 Hz, 2H), 3.40 (d, *J*=6.8 Hz, 1H), 3.37 (s, 3H), 3.33 (d, *J*=6.2 Hz, 2H), 3.3 (s, 3H), 2.93-2.86 (m, 3H), 2.04-1.84 (m, 9H), 1.57-1.41 (m, 2H), 1.39 (d, *J*=6.8 Hz, 6H)
267	(400 MHz, $CDCl_3$) δ ppm 8.04 (d, *J*=7.6 Hz, 2H), 7.57-7.53 (m, 2H), 7.45 (s, 1H), 7.37-7.33 (m, 1H), 4.02-3.78 (m, 2H), 3.72-3.67 (m, 5H), 3.40-3.36 (m, 9H), 2.98-2.91 (m, 2H), 2.90-2.86 (m, 2H), 2.72-2.60 (m, 3H), 2.50-2.37 (m, 7H), 2.10-2.02 (m, 2H), 1.95 (d, *J*=13.3 Hz, 2H)
269	(400 MHz, $CDCl_3$) δ ppm 10.01 (br. s, 1 H), 8.33 - 8.40 (m, 2 H), 8.03 (s, 1 H), 7.79 (br. s, 1 H), 7.69 (dd, *J*=8.8, 2.5 Hz, 1 H), 7.57 (dd, *J*=5.5, 1.6 Hz, 1 H), 6.85 (d, *J*=8.7 Hz, 1 H), 3.90 - 4.05 (m, 6 H), 3.61 - 3.75 (m, 6 H), 3.49 (s, 3 H), 3.19 - 3.31 (m, 1 H), 3.00 (s, 1 H), 1.96 - 2.17 (m, 4 H), 1.27 (d, J=6.8 Hz, 6 H)

Cpd Number	^{1}H NMR data
270	(400 MHz, $CDCl_3$) δ ppm 8.05 (dd, J=8.6, 1.1 Hz, 2 H), 7.58 (dd, J=8.3, 7.6 Hz, 2 H), 7.47 (s, 1 H), 7.33 - 7.42 (m, 1 H), 4.02 (s, 1 H), 3.42 (s, 3 H), 3.33 - 3.39 (m, 4 H), 2.76 - 2.86 (m, 5 H), 2.56 - 2.71 (m, 2 H), 2.40 - 2.50 (m, 2 H), 2.03 - 2.16 (m, 2 H), 1.16 (d, J=6.5 Hz, 6 H)
271	(400 MHz, $CDCl_3$) δ ppm 8.06 (d, *J*=8.44 Hz, 2H), 7.56 (t, *J*=7.72 Hz, 2H), 7.45 (s, 1H), 7.38-7.34 (m, 1H), 7.26 (s, 1H), 4.05-3.96 (m, 1H), 3.87 (t, *J*=5.76 Hz, 2H), 3.78 (t, *J*=11.48 Hz, 2H), 3.36 (t, *J*=3.8 Hz, 4H), 3.26 (s, 3H), 2.84-2.78 (m, 5H), 2.67-2.58 (m, 2H), 2.47-2.40 (m, 2H), 2.13-2.04 (m, 2H), 1.14 (d, *J*=6.48 Hz, 6H)
272	(400 MHz, $CDCl_3$) δ ppm 7.98-7.94 (m, 2H), 7.50 (s, 1H), 7.23 (d, *J*=8.72 Hz, 2H), 3.79 (d, *J*=11.8 Hz, 1H), 3.71-3.64 (m, 8H), 3.49-3.41 (m, 1H), 3.39 (s, 3H), 3.35 (d, *J*=6.2 Hz, 2H), 2.97 (t, *J*=11.32 Hz, 2H), 2.48 (t, *J*=6.8 Hz, 2H), 2.44-2.37 (m, 4H), 2.10-2.03 (m, 2H), 1.95 (d, *J*=13.12 Hz, 3H), 1.59-1.52 (m, 2H), 1.46 (d, *J*=6.76 Hz, 6H)
273	(400 MHz, $CD_3OD/CDCl_3$) δ ppm 8.01 (d, J=7.9 Hz, 2H), 7.50 (m, 2H), 7.46 (s, 1H), 7.32 (t, *J*=7.6 Hz, 1H), 4.00 (pent, J=8.5, 1H), 3.67-3.60 (m, 2H), 3.48 (t, J=6.4 Hz, 2H), 3.40-3.36 (m, 5H), 3.21 (t, J=6.4, 2H), 2.94-2.85 (m, 2H), 2.62-2.50 (m, 2H), 2.45 (s, 6H), 2.44-2.35 (m, 2H), 2.13-2.80 (m, 5H), 1.60-1.49 (m, 2H);

Cpd Number	^{1}H NMR data
274	(400 MHz, $CDCl_3$) δ ppm 10.00 (m, 1H-NH), 8.03 (dd, *J*=1.2, 8.7 Hz, 2H), 7.59-7.54 (m, 2H), 7.47 (s, 1H), 7.39-7.35 (m, 1H), 7.26 (s, 1H), 4.84-4.69 (m, 1H), 4.67-4.60 (m, 1H), 4.30 (d, *J*=18.3, 2H), 4.04 (dt, *J*=8.4, 16.8 Hz, 1H), 3.87-3.79 (m, 1H), 3.58-3.49 (m, 1H), 3.42 (s, 3H), 3.10 (s, 3H), 3.08-2.99 (m, 1H), 2.6-2.5 (m, 2H), 2.49-2.39 (m, 2H), 2.16 (s, 2H), 2.15-2.07 (m, 2H)
275	(400 MHz, $CDCl_3$) δ ppm 8.56 (s, 1 H), 7.99 (br. s., 3 H), 7.90 (d, *J* = 8.5 Hz, 1 H), 7.46 (br. s., 2 H), 7.34-7.25 (m, 1 H), 6.74 (d, *J* = 8.7 Hz, 1 H), 5.56 (br. s., 1 H), 4.98 (br. s., 4 H), 4.11-4.04 (m, 1 H), 4.01-3.90 (m, 1 H), 3.90-3.81 (m, 2 H), 3.72 (d, *J* = 3.6 Hz, 1 H), 3.68-3.58 (m, 1H), 3.40 (s, 3 H), 3.36 (t, *J* = 5.5 Hz, 2 H), 3.26 (s, 2 H), 3.01-2.89 (m, 1 H), 2.37-2.21 (m, 2 H), 2.11-1.88 (m, 2 H) (NH missing)
276	(400 MHz, $CDCl_3$) δ ppm 8.29 (d, *J* = 2.2 Hz, 1 H), 8.13 (d, *J* = 7.7 Hz, 2 H), 7.98-7.92 (m, 1 H), 7.63 (dd, *J* = 8.9, 2.4 Hz, 1 H), 7.58-7.49 (m, 2 H), 7.36 (d, *J* = 7.5 Hz, 1 H), 6.80 (d, *J* = 8.9 Hz, 1 H), 3.97 (ddd, *J* = 13.6, 7.2, 3.6 Hz, 2 H), 3.87 (t, *J* = 6.7 Hz, 2 H), 3.71-3.58 (m, 5 H), 3.33 (s, 3 H), 2.96 (dt, *J* = 7.9, 3.8 Hz, 1 H), 2.81 (q, *J* = 7.1 Hz, 2 H), 2.55-2.41 (m, 2 H), 2.12-1.93 (m, 3 H), 1.77-1.65 (m, 2 H), 1.08 (d, *J* = 6.3 Hz, 3 H) (NH missing)
277	(400 MHz, $CDCl_3$) δ ppm 8.59-8.54 (m, 1H), 8.05-7.87 (m, 4H), 7.62-7.46 (m, 2H), 7.38-7.28 (m, 1H), 6.78-6.69 (m, 2H), 4.12-4.03 (m, 2H), 4.00-3.87 (m, 5H), 3.78-3.56 (m, 2H), 3.48-3.38 (m, 2H), 3.38-3.30 (m, 1H), 2.97-2.89 (m, 1H), 2.09-1.89 (m, 6H)

Cpd Number	^{1}H NMR data
278	(300 MHz, $CDCl_3$) δ ppm 7.49-7.46 (m, 2H), 7.41-7.29 (m,2H), 6.73-6.68 (m, 1H), 4.17 (d, *J*=6.3 Hz, 2H), 4.08 (dd, *J*=3.3, 11.4 Hz, 2H), 3.61-3.45 (m, 3H), 3.40 (s, 3H), 3.06 (m, 6H), 1.82 (dd, *J*=1.77, 12.8 Hz, 2H), 1.67-1.50 (m, 4H), 1.47 (d, *J*=6.9, 6H)
279	(400 MHz, $CDCl_3$) δ ppm 10.34-10.25 (m, 1H), 8.42 (d, *J*=5.4 Hz, 1H), 7.60 (s, 1H), 7.24 (d, *J*=5.4 Hz, 1H), 3.89 (dt, *J*=4.3, 8.6 Hz, 8H), 3.65 (d, *J*=12 Hz, 2H), 3.49-3.41 (m, 1H), 3.39 (s, 3H), 3.40 (s, 3H), 3.35 (d, *J*=6.2 Hz, 2H), 2.97 (t, *J*=11.8 Hz, 2H), 1.94 (d, *J*=5.4 Hz, 2H), 1.57-1.50 (m, 1H), 1.45 (d, *J*=6.7 Hz, 6H), 1.34-1.18 (m,2H)
281	(400 MHz, $CDCl_3$) δ ppm 8.04 (dt, *J*=1.2, 3.1 Hz, 2H), 7.56 (t, *J*=7.7 Hz, 2H), 7.50 (s, 1H), 7.38-7.33 (m, 1H), 7.26 (s,1H), 4.38 (t, *J*=6.4 Hz, 2H), 4.11 (q, *J*=8.3, 16.8 Hz, 1H), 3.75 (t, *J*=4.6, 9.3 Hz, 4H), 3.42 (s, 3H), 2.63-2.38 (m, 8H), 2.19-1.94 (m, 6H)
282	(400 MHz, $CDCl_3$) δ ppm 10.03 (br. s, 1 H), 8.06 (d, J=7.7 Hz, 2 H), 7.58 (t, J=7.9 Hz, 2 H), 7.50 (s, 1 H), 7.35 - 7.42 (m, 1 H), 4.21 (s, 2 H), 4.08 (t, J=8.4 Hz, 1 H), 3.44 (s, 3 H), 2.81 (d, J=13.7 Hz, 2 H), 2.38 - 2.63 (m, 4 H), 2.13 (d, J=8.9 Hz, 2 H), 1.52 (s, 3 H)
283	(400 MHz, $CDCl_3$) δ ppm 8.06 (dd, *J*=8.6, 1.1 Hz, 2 H), 7.57 (t, *J*=7.9 Hz, 2 H), 7.51 (s, 1 H), 7.33 - 7.41 (m, 1 H), 4.39 - 4.49 (m, 1 H), 4.31 (m, *J*=5.1, 5.1 Hz, 2 H), 4.10 (m, *J*=8.7 Hz, 1 H), 3.85 - 4.02 (m, 2 H), 3.43 (s, 3 H), 2.40 - 2.66 (m, 4 H), 1.95 - 2.27 (m, 5 H), 1.81 - 1.94 (m, 1 H)

Cpd Number	^{1}H NMR data
286	(400 MHz, $CDCl_3$) δ ppm 10.00 (s, 1H-NH), 7.97 (d, J=7.9, 2H), 7.72 (d, *J*=1.5 Hz, 1H), 7.55 (t, *J*=7.9 Hz, 2H), 7.47 (s, 1H), 7.37 (t, *J*=8.8 Hz, 2H), 3.98 (pent, J=8.5 Hz, 1H), 3.70 (s, 3H), 3.64-3.57 (m, 2H), 3.39 (s, 3H), 3.35 (d, *J*=6.3 Hz, 2H), 2.90-2.81 (m, 2H), 2.64-2.53 (m, 2H), 2.44-2.34 (m, 2H), 2.13-1.77 (m, 5H), 1.58-1.47 (m, 2H)
287	(400 MHz, $CDCl_3$) δ ppm 10.35 (s, 1 H), 7.95 (d, J=8.0 Hz, 2 H), 7.58 (t, J=7.5 Hz, 2 H), 7.45-7.38 (m, 1 H), 7.40 (s, 1 H), 3.98 (pent, J=8.3 Hz, 1 H), 3.68-3.60 (m, 2 H), 3.39 (s, 3 H), 3.36 (d, J=6.6 Hz, 2 H), 2.95-2.86 (m, 2 H), 2.76 (s, 3H), 2.65-2.54 (m, 2 H), 2.46-2.36 (m, 2 H), 2.44 (s, 3H), 2.17-2.01 (m, 2 H), 2.00-1.82 (m, 3 H), 1.60-1.48 (m, 2 H)
288	(400 MHz, $CDCl_3$) δ ppm 9.96 (s, 1 H), 8.04 (d, J=7.9 Hz, 2 H), 7.56 (t, J=7.9 Hz, 2 H), 7.45 (s, 1 H), 7.36 (t, J=7.5 Hz, 1 H), 3.98 (pent, J=8.5 Hz, 1 H), 3.89 (t, J=7.5 Hz, 2 H), 3.70-3.65 (m, 2 H), 3.67 (s, 3 H), 3.40 (s, 3 H), 3.37 (d, J=6.2 Hz, 2 H), 3.0-2.89 (m, 4 H), 2.69-2.57 (m, 2 H), 2.48-2.38 (m, 2 H), 2.14-2.01 (m, 2 H), 2.00-1.82 (m, 3 H), 1.64-1.51 (m, 2 H)
289	(400 MHz, $CDCl_3$) δ ppm 9.94 (s, 1 H), 8.04 (d, J= Hz, 2 H), 7.55 (t, J=7.9 Hz, 2 H), 7.44 (s, 1 H), 7.35 (t, J=7.5 Hz, 1 H), 3.97 (pent, J=8.4 Hz, 1 H), 3.85 (t, J=7.5 Hz, 2 H), 3.71-3.65 (m, 2 H), 3.40 (s, 3 H), 3.37 (d, J=6.3 Hz, 2 H), 2.99-2.91 (m, 4 H), 2.68-2.56 (m, 2 H), 2.47-2.37 (m, 2 H), 2.15-2.00 (m, 2 H), 1.99-1.82 (m, 3 H), 1.63-1.50 (m, 2 H)

Cpd Number	^{1}H NMR data
290	(400 MHz, $CDCl_3$) δ ppm 8.01-7.98 (m, 2H), 7.51 (s, 1H), 7.21 (t, J=8.5 Hz, 2H), 3.99-3.71 (m, 1H), 3.67 (d, J=12.4 Hz, 2H), 3.58 (t, J=15.4 Hz, 2H), 3.48-3.42 (m, 1H), 3.38 (s, 3H), 3.34 (d, J=6.3 Hz, 2H), 2.94 (t, J=12.0 Hz, 2H), 2.55 (t, J=6.9 Hz, 2H), 2.28 (s, 6H), 2.25-2.21 (m, 1H), 2.09 (quint, J=6.9, 14.5, 2H), 1.93 (d, J=13.2 Hz, 2H), 1.58-1.49 (m, 2H), 1.45 (d, J=6.8 Hz, 6H),
291	(400 MHz, $CDCl_3$) δ ppm 8.03 (br. s., 2 H), 7.55 (s, 1 H), 7.13 (br. s., 2 H), 3.63 (d, *J*=12.0 Hz, 2 H), 3.25 - 3.54 (m, 8 H), 3.11 (d, *J*=2.9 Hz, 6 H), 2.82 - 2.98 (m, 2 H), 2.35 (quin, *J*=7.4 Hz, 2 H), 1.78 - 1.97 (m, 7 H), 1.37 - 1.63 (m, 8 H)
294	(400 MHz, $CDCl_3$) δ ppm 10.07 (m, 1H-NH), 8.04 (d, *J*=7.5 Hz, 2H), 7.55 (t, *J*=7.6 Hz, 2H), 7.45 (s, 1H), 7.35 (tt, *J*=1.12, 7.2 Hz, 1H), 3.98 (q, *J*=8.3, 16.7 Hz, 1H), 3.74 (d, *J*=12.7 Hz, 2H), 3.4 (s, 3H), 3.24 (s, 3H), 2.9 (t, *J*=11.6 Hz, 2H), 2.67-2.57 (m, 2H), 2.46-2.40 (m, 2H), 2.11-2.03 (m, 2H), 1.91 (d, *J*=10.5 Hz, 2H), 1.70-1.59 (m, 3H), 1.20 (s, 6H)
296	(400 MHz, $CDCl_3$) δ ppm 10.02 (m, 1H-NH), 8.03 (dd, J=1.2, 8.7 Hz, 2H), 7.55 (t, J=7.9 Hz, 2H), 7.45 (s, 1H), 7.36 (tt, J=1.0, 7.0 Hz, 1H), 4.76 (d, J=1.9 Hz, 1H), 4.17 (d, J=6.2 Hz, 2H), 4.03 (q, J=8.4, 17 Hz, 1H), 3.94 (d, J=1.6 Hz, 1H), 3.42 (s, 3H), (td, J=2.5, 13.4 Hz, 1H), 2.69-2.51 (m, 3H), 2.46-2.38 (m, 2H), 2.14 (s, 3H), 2.11-2.08 (m, 1H), 2.04-1.90 (m, 4H), 1.49-1.35 (m, 2H)

Cpd Number	^{1}H NMR data
297	(400 MHz, $CDCl_3$) δ ppm 10.02 (m, 1H-NH), 8.03 (dd, J=1.6, 11.7 Hz, 2H), 7.56 (t, J=10.2 Hz, 2H), 7.45 (s, 1H), 7.36 (t, J=9.9 Hz, 1H), 4.37-4.20 (m, 2H), 4.16 (d, J=8.3 Hz, 1H), 4.04 (q, J=11.3, 22.6 Hz, 1H), 3.72 (s, 3H), 3.42 (s, 3H), 2.87 (t, J=15.7 Hz, 2H), 2.63-2.50 (m, 2H), 2.48-2.37 (m, 2H), 2.2-1.95 (m, 3H), 1.90 (d, J=17.4 Hz, 2H), 1.50-1.23 (m, 3H),
298	(400 MHz, $CDCl_3$/CD_3OD) δ ppm 7.99 (d, J=8.25, 2H), 7.51 (t, *J*=8.0 Hz, 2H), 7.44 (s, 1H), 7.32 (t, J=7.4, 1H), 3.98 (pent, *J*=8.4 Hz, 1H), 3.67-3.59 (m, 2H), 3.50 (t, J=6.5 Hz, 2H), 3.40-3.33 (m, 2H), 3.37 (s, 3H), 3.14 (t, *J*=6.5 Hz, 2H), 2.94-2.84 (m, 2H), 2.6-2.49 (m, 2H), 2.44-2.34 (m, 2H), 2.38 (s, 6H), 2.12-1.79 (m, 5H), 1.60-1.48 (m, 2H)
300	(400 MHz, $CDCl_3$) δ ppm 9.89 (m, 1H-NH), 8.65 (bs, 1H), 8.09-8.03 (m, 1H), 7.99-7.94 (m, 3H), 7.58-7.51 (m, 2H), 7.37-7.33 (m, 1H), 6.83-6.78 (m, 1H), 5.76-5.71 (m, 1H), 5.06 (t, J=6.0 Hz, 2H), 4.81 (t, J=6.3 Hz, 2H), 4.03-3.95 (m, 2H), 3.72-3.65 (m, 2H), 3.45 (bs, 3H), 3.00-2.93 (m, 1H), 2.12-1.95 (m, 4H);
301	(400 MHz, $CDCl_3$) δ ppm 8.01-7.92 (m, 2 H), 7.49 (s, 1 H), 7.24 (t, *J* = 8.7 Hz, 2 H), 3.68-3.61 (m, 4 H), 3.56-3.45 (m, 1 H), 3.41 (s, 3 H), 3.31 (s, 3 H), 3.17 (s, 3 H), 1.48-1.40 (m, 6 H)
302	(400 MHz, $CDCl_3$) δ ppm 8.02 (dd, *J*=8.3, 4.6 Hz, 2 H), 7.53 (s, 1 H), 7.16 - 7.25 (m, 2 H), 3.42 - 3.71 (m, 10 H), 3.39 (s, 3 H), 3.35 (d, *J*=6.4 Hz, 2 H), 2.82 - 2.97 (m, 4 H), 2.11 - 2.21 (m, 2 H), 2.02 (quin, *J*=7.0 Hz, 2 H), 1.92 (d, *J*=13.0 Hz, 2 H), 1.81 - 1.87 (m, 1 H), 1.50 - 1.59 (m, 2 H), 1.46 (d, *J*=6.6 Hz, 6 H)

Cpd Number	^{1}H NMR data
303	(400 MHz, $CDCl_3$) δ ppm 8.06 (d, *J*=7.5 Hz, 2 H), 7.57 (t, *J*=7.9 Hz, 2 H), 7.51 (s, 1 H), 7.37 (s, 1 H), 4.39 (t, *J*=6.4 Hz, 2 H), 4.03 - 4.14 (m, 1 H), 3.43 (s, 3 H), 2.53 - 2.65 (m, 4 H), 2.40 - 2.51 (m, 2 H), 2.32 (s, 6 H), 2.08 - 2.22 (m, 3 H), 1.96 - 2.07 (m, 1 H)
304	(400 MHz, $CDCl_3$) δ ppm 9.98 (m, 1H-NH), 7.97-7.93 (m, 2H), 7.51 (s, 1H), 7.27-7.20 (m, 2H), 3.76 (d, J=12.5 Hz, 2H), 3.50-3.42 (m, 1H), 3.40 (s, 3H), 2.93 (t, J=11.8 Hz, 2H), 1.97 (d, J=11.6 Hz, 2H), 1.70-1.50 (m, 4H), 1.47 (s,3H), 1.45 (s, 3H), 1.27 (d, J=6.7,6H)
314	(400 MHz, $CDCl_3$) δ ppm 8.06 (dd, J=8.6, 1.1 Hz, 2 H), 7.57 (t, J=7.9 Hz, 2 H), 7.49 (s, 1 H), 7.33 - 7.40 (m, 1 H), 4.37 (t, J=6.3 Hz, 2 H), 4.07 (s, 1 H), 3.43 (s, 3 H), 2.38 - 2.64 (m, 10 H), 1.93 - 2.24 (m, 4 H), 1.58 - 1.71 (m, 4 H), 1.50 (d, J=4.9 Hz, 2 H)
315	(400 MHz, DMSO-d_6) δ ppm 8.31 – 8.22 (m, 2H), 7.61 – 7.51 (m, 2H), 7.41 – 7.30 (m, 2H), 4.19 (d, *J* = 6.1 Hz, 2H), 4.05 – 3.87 (m, 3H), 3.83 – 3.72 (m, 4H), 3.38 (td, *J* = 11.7, 2.0 Hz, 2H), 3.16 (s, 3H), 2.51 – 2.31 (m, 5H), 2.19 – 1.98 (m, 2H), 1.78 – 1.68 (m, 2H), 1.44 (qd, *J* = 12.1, 4.5 Hz, 2H)
316	(400 MHz, $CDCl_3$) δ ppm 7.96 - 8.05 (m, 2 H), 7.47 (s, 1 H), 7.22 - 7.32 (m, 2 H), 3.99 (quin, *J*=8.4 Hz, 1 H), 3.71 (d, *J*=12.5 Hz, 2 H), 3.37 - 3.44 (m, 8 H), 2.98 (td, *J*=12.3, 2.1 Hz, 2 H), 2.57 - 2.68 (m, 2 H), 2.39 - 2.51 (m, 2 H), 2.38 - 2.50 (m, 2 H), 2.04 - 2.13 (m, 2 H), 1.97 (d, *J*=13.0 Hz, 2 H), 1.62 (dd, *J*=12.3, 3.5 Hz, 2 H)

Cpd Number	^{1}H NMR data
317	(400 MHz, $CDCl_3$) δ ppm 10.06 (br. s., 1 H), 8.06 (d, *J*=2.7 Hz, 2 H), 7.58 (t, *J*=3.2 Hz, 2 H), 7.48 (s, 1 H), 7.38 (t, *J*=1.2 Hz, 1 H), 3.93 - 4.08 (m, 1 H), 3.78 (d, *J*=12.7 Hz, 2 H), 3.38 - 3.47 (m, 3 H), 2.94 (t, *J*=11.6 Hz, 2 H), 2.58 - 2.71 (m, 2 H), 2.40 - 2.51 (m, 2 H), 1.96 - 2.16 (m, 4 H), 1.59 - 1.76 (m, 3 H), 1.30 (s, 6 H)
318	(400 MHz, $CDCl_3$) δ ppm 7.92 - 8.08 (m, 2 H), 7.48 (s, 1 H), 7.19 - 7.34 (m, 2 H), 4.17 (d, *J*=6.4 Hz, 2 H), 4.03 - 4.12 (m, 2 H), 3.52 (td, *J*=11.8, 2.1 Hz, 2 H), 3.43 (s, 3 H), 2.52 - 2.64 (m, 2 H), 2.40 - 2.50 (m, 2 H), 2.19 - 2.33 (m, 1 H), 2.10 - 2.18 (m, 1 H), 1.98 - 2.07 (m, 1 H), 1.83 (dd, *J*=13.0, 2.0 Hz, 2 H), 1.53 - 1.66 (m, 4 H)
319	(300 MHz, $CDCl_3$) δ ppm 7.92 - 8.02 (m, 2 H), 7.53 (s, 1 H), 7.21 - 7.29 (m, 2 H), 3.45 - 3.55 (m, 1 H), 3.31 - 3.44 (m, 7 H), 2.72 - 2.88 (m, 5 H), 1.48 (d, *J*=6.7 Hz, 6 H), 1.14 (d, *J*=6.5 Hz, 6 H)
320	(300 MHz, $CDCl_3$) δ ppm 7.97 - 8.07 (m, 2 H), 7.49 (s, 1 H), 7.23 (d, *J*=9.1 Hz, 2 H), 3.70 (d, *J*=12.3 Hz, 2 H), 3.37 - 3.48 (m, 4 H), 3.25 - 3.36 (m, 2 H), 2.90 (t, *J*=11.7 Hz, 2 H), 2.54 - 2.65 (m, 3 H), 2.31 (d, *J*=13.5 Hz, 2 H), 1.78 - 1.95 (m, 4 H), 1.67 (d, *J*=11.7 Hz, 1 H), 1.23 - 1.53 (m, 11 H)
323	(400 MHz, $CDCl_3$) δ ppm 8.04 - 8.12 (m, 2 H), 7.55 (t, *J*=7.9 Hz, 2 H), 7.48 (s, 1 H), 7.32 - 7.38 (m, 1 H), 4.28 - 4.39 (m, 2 H), 4.04 (t, *J*=8.6 Hz, 1 H), 3.40 (s, 3 H), 2.99 - 3.09 (m, 1 H), 2.48 - 2.63 (m, 2 H), 2.44 - 2.48 (m, 3 H), 2.28 - 2.44 (m, 5 H), 1.93 - 2.18 (m, 3 H), 1.81 (d, *J*=10.6 Hz, 2 H), 1.61 - 1.72 (m, 2 H), 1.47 - 1.59 (m, 1 H), 1.24 - 1.44 (m, 1 H)

Cpd Number	^{1}H NMR data
324	(400 MHz, $CDCl_3$) δ ppm 10.05 (br. s, 1 H), 8.05 (d, *J*=11.1 Hz, 2 H), 7.61 (s, 1 H), 7.57 (t, *J*=7.9 Hz, 2 H), 7.37 (s, 1 H), 4.97 - 5.05 (m, 1 H), 4.03 - 4.15 (m, 1 H), 3.76 (d, *J*=4.9 Hz, 3 H), 3.38 - 3.47 (m, 6 H), 2.60 (s, 2 H), 2.37 - 2.51 (m, 2 H), 2.08 - 2.23 (m, 1 H), 1.91 - 2.07 (m, 1 H), 1.56 - 1.68 (m, 1 H)
325	(400 MHz, $CDCl_3$) δ ppm 9.72 - 10.33 (m, 1 H), 7.98 - 8.12 (m, 2 H), 7.53 - 7.63 (m, 2 H), 7.51 (s, 1 H), 7.32 - 7.41 (m, 1 H), 4.72 (quin, *J*=6.8 Hz, 5 H), 4.18 - 4.35 (m, 4 H), 4.11 (s, 1 H), 3.44 (s, 3 H), 3.22 (t, *J*=6.5 Hz, 2 H), 2.95 - 3.09 (m, 1 H), 2.52 - 2.64 (m, 2 H), 2.40 - 2.52 (m, 2 H), 2.14 (s, 1 H), 2.02 (s, 1 H), 1.05 (d, *J*=6.7 Hz, 6 H)
326	(400 MHz, $CDCl_3$) δ ppm 10.03 (br. s., 1 H), 8.06 (dd, J=8.7, 1.1 Hz, 2 H), 7.59 (t, J=8.1 Hz, 2 H), 7.53 (s, 1 H), 7.40 (t, J=8.1 Hz, 1 H), 3.96 (m, J=8.6, 8.6 Hz, 1 H), 3.48 - 3.57 (m, 2 H), 3.44 (s, 3 H), 3.34 - 3.41 (m, 2 H), 2.72 (s, 2 H), 2.59 - 2.69 (m, 2 H), 2.44 (m, J=8.7, 3.8 Hz, 2 H), 1.98 - 2.15 (m, 6 H)
328	(501 MHz, DMSO-d_6) δ ppm 8.37-8.33 (m, 2H), 7.59-7.54 (m, 2H), 7.37-7.33 (m, 1H), 7.30 (s, 1H), 3.99 (tt, J = 8.3, 8.3 Hz, 1H), 3.71-3.65 (m, 4H), 3.65-3.59 (m, 2H), 3.24 (s, 3H), 3.18-3.16 (m, 1H), 2.98-2.91 (m, 2H), 2.80-2.62 (m, 5H), 2.56-2.39 (m, 3H), 2.13-1.94 (m, 4H), 1.78-1.68 (m, 2H)
331	(400 MHz, DMSO-d_6) δ ppm 8.38-8.33 (m, 2H), 7.59-7.53 (m, 2H), 7.36-7.31 (m, 1H), 7.30 (s, 1H), 3.98 (tt, J = 8.4, 8.3 Hz, 1H), 3.69 (t, J = 4.7 Hz, 4H), 3.56-3.50 (m, 2H), 3.19-3.16 (m, 3H), 2.92-2.82 (m, 2H), 2.82-2.68 (m, 6H), 2.56-2.34 (m, 4H), 2.09-1.92 (m, 2H), 1.90-1.82 (m, 2H), 1.63-1.38 (m, 5H)

Cpd Number	^{1}H NMR data
332	(501 MHz, CD_2Cl_2) δ ppm 8.11-8.07 (m, 2H), 7.60-7.54 (m, 2H), 7.50-7.46 (m, 1H), 7.40-7.35 (m, 1H), 4.30-3.93 (m, 2H), 3.73-3.35 (m, 11H), 3.03-2.86 (m, 1H), 2.73-2.21 (m, 13H), 2.17-1.93 (m, 9H)
333	(400 MHz, DMSO-d_6) δ ppm 8.31 – 8.23 (m, 2H), 7.62 – 7.53 (m, 2H), 7.41 – 7.32 (m, 2H), 4.22 (d, J = 6.1 Hz, 2H), 4.05 – 3.88 (m, 3H), 3.39 (td, J = 11.7, 2.0 Hz, 2H), 3.11 (s, 1H), 2.52 – 2.33 (m, 7H), 2.19 – 1.85 (m, 4H), 1.79 – 1.69 (m, 2H), 1.46 (qd, J = 12.2, 4.4 Hz, 2H), 1.23 (qd, J = 5.1, 2.3 Hz, 2H), 1.15 (qdd, J = 6.3, 4.7, 1.4 Hz, 2H)
334	(400 MHz, DMSO-d_6) δ ppm 8.34 – 8.23 (m, 2H), 7.62 – 7.50 (m, 2H), 7.42 – 7.31 (m, 2H), 4.21 (d, J = 6.2 Hz, 2H), 4.07 – 3.88 (m, 3H), 3.39 (td, J = 11.7, 2.0 Hz, 2H), 2.92 (s, 5H), 2.52 – 2.32 (m, 7H), 2.07 (ddd, J = 17.5, 8.8, 2.0 Hz, 2H), 2.03 – 1.87 (m, 1H), 1.74 (d, J = 12.9 Hz, 2H), 1.45 (qd, J = 12.3, 4.5 Hz, 2H)
335	(400 MHz, DMSO-d_6) δ ppm 8.31 – 8.21 (m, 2H), 7.62 – 7.51 (m, 2H), 7.41 – 7.31 (m, 2H), 4.19 (d, J = 6.1 Hz, 2H), 4.04 – 3.87 (m, 3H), 3.54 (q, J = 7.4 Hz, 2H), 3.38 (td, J = 11.7, 2.1 Hz, 2H), 2.49 – 2.31 (m, 4H), 2.12 – 1.98 (m, 2H), 1.98 – 1.84 (m, 1H), 1.77 – 1.68 (m, 2H), 1.44 (qd, J = 12.2, 4.5 Hz, 2H), 1.29 (t, J = 7.4 Hz, 3H)
336	(400 MHz, $CDCl_3$) δ ppm 10.00 (br. s., 1 H), 8.32 (d, J=5.6 Hz, 1 H), 7.72 (d, J=1.5 Hz, 1 H), 7.55 (s, 1 H), 7.51 (dd, J=5.6, 1.7 Hz, 1 H), 4.20 (d, J=6.4 Hz, 2 H), 4.05 - 4.13 (m, 2 H), 3.85 - 3.93 (m, 4 H), 3.59 - 3.65 (m, 4 H), 3.47 - 3.59 (m, 3 H), 3.43 - 3.46 (m, 3 H), 2.18 - 2.32 (m, 1 H), 1.82 (dd, J=12.7, 2.0 Hz, 2 H), 1.53 - 1.66 (m, 2 H), 1.47 (d, J=6.8 Hz, 6 H)

Cpd Number	^{1}H NMR data
337	(400 MHz, $CDCl_3$) δ ppm 10.09 -9.88 (m, 1 H), 8.04 - 7.91 (m, 2 H), 7.56 (s, 1 H), 7.34- 7.18 (m, 2 H), 4.22 (q, *J*=7.1 Hz, 2 H), 3.87 -3.67 (m, 4 H), 3.53-3.36 (m, 4 H), 3.35 -3.25 (m, 4 H), 1.49 (d, *J*=6.9 Hz, 6 H), 1.40 -1.23 (m, 3 H)
338	(400 MHz, DMSO-d_6) δ ppm 8.37- 8.26 (m, 2 H), 7.48 - 7.32 (m, 3 H), 3.55 -3.38 (m, 8 H), 3.35 (m., 2 H), 2.80 (s, 3 H), 2.04 (t, *J*=5.2 Hz, 4 H), 1.43 (d, *J*=6.7 Hz, 6 H)
339	(300 MHz, $CDCl_3$) δ ppm 8.02-7.88 (m, 2 H), 7.59 (s, 1 H), 7.34 -7.19 (m, 2 H), 3.81 -3.00 (m, 11 H), 1.49 (dd, *J*=6.7, 4.9 Hz, 6 H)
340	(400 MHz, DMSO-d_6) δ ppm 8.38 -8.26 (m, 2 H), 7.46 - 7.31 (m, 3 H), 3.56 (t, *J*=5.5 Hz, 2 H), 3.51 -3.39 (m, 1 H), 3.37 -3.21 (m, 10 H), 2.90 (m., 6 H), 1.42 (d, *J*=6.9 Hz, 6 H)
341	(400 MHz, $CDCl_3$) δ ppm 8.01 -7.90 (m, 2 H), 7.62 (s, 1 H), 7.32 -7.22 (m, 2 H), 4.74 (s., 2 H), 3.84-3.69 (m, 2 H), 3.49- 3.38 (m, 4 H), 3.32 -3.20 (m, 2 H), 2.46 -2.31 (m, 2 H), 2.00 (d, *J*=13.7 Hz, 2 H), 1.54 -1.47 (m, 6 H)
347	(501 MHz, DMSO-d_6) δ ppm 8.37 (d, J = 8.0 Hz, 2H), 7.59 7.53 (m, 2H), 7.39 (s, 1H), 7.33 (t, J = 7.4 Hz, 1H), 4.20 (d, J = 6.1 Hz, 2H), 4.02 (p, J = 8.4 Hz, 1H), 3.97 3.91 (m, 2H), 3.64 3.58 (m, 4H), 3.44 3.37 (m, 4H), 2.76 2.59 (m, 6H), 2.5 2.35 (m, 4H), 2.23 2.02 (m, 2H), 1.99 1.90 (m, 3H), 1.80 1.73 (m, 2H), 1.53 1.42 (m, 2H)

Cpd Number	^{1}H NMR data
348	(400 MHz, $CDCl_3$) δ ppm 7.94 - 8.03 (m, 2 H), 7.51 (s, 1 H), 7.18 - 7.26 (m, 2 H), 3.67 - 3.77 (m, 2 H), 3.46 (dt, *J*=13.5, 6.8 Hz, 1 H), 3.40 (s, 3 H), 2.94 (t, *J*=11.7 Hz, 2 H), 2.65 (br. s., 4 H), 2.54 (ddd, *J*=11.3, 7.9, 3.5 Hz, 1 H), 2.03 - 2.14 (m, 2 H), 1.82 (qd, *J*=12.1, 3.4 Hz, 2 H), 1.69 (quin, *J*=5.5 Hz, 4 H), 1.40 - 1.55 (m, 8 H)
349	(400 MHz, CD_2Cl_2) δ ppm 8.11-8.05 (m, 2H), 7.59-7.51 (m, 2H), 7.48 (s, 1H), 7.34 (t, J = 7.4 Hz, 1H), 6.71 (bs, 1H), 4.03 (p, J = 8.4 Hz, 1H), 3.78-3.71 (m, 1H), 3.67-3.52 (m, 3H), 3.35 (s, 3H), 2.97-2.88 (m, 1H), 2.80-2.72 (m, 1H), 2.69-2.41 (m, 4H), 2.15-1.79 (m, 6H), 1.33-1.20 (m, 1H)
350	(501 MHz, DMSO-d_6) δ ppm 8.38-8.34 (m, 2H), 7.58-7.54 (m, 2H), 7.34 (t, J = 7.4 Hz, 1H), 7.29 (s, 1H), 4.67 (bs, 1H), 4.02 (p, J = 8.3 Hz, 1H), 3.66-3.61 (m, 1H), 3.61-3.57 (m, 4H), 3.53-3.41 (m, 4H), 3.35-3.30 (m, 1H), 2.88-2.81 (m, 1H), 2.66-2.38 (m, 11H), 2.11-2.01 (m, 1H), 2.00-1.58 (m, 7H), 1.22-1.12 (m, 1H)
351	(400 MHz, pyridine-d_5) δ ppm 8.39 – 8.32 (m, 2H), 7.61 (s, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.24 (td, *J* = 7.5, 1.3 Hz, 1H), 3.52 – 3.33 (m, 5H), 2.68 (dq, *J* = 11.3, 8.8 Hz, 2H), 2.54 (dq, *J* = 8.5, 3.9 Hz, 2H), 2.44 (s, 4H), 2.18 (s, 4H), 1.78 – 1.68 (m, 4H), 1.63 – 1.52 (m, 6H)
352	(400 MHz, pyridine-d_5) δ ppm 8.61 (d, *J* = 7.7 Hz, 2H), 7.66 (s, 1H), 7.51 (d, *J* = 1.8 Hz, 2H), 7.36 – 7.20 (m, 1H), 5.41 (dd, *J* = 8.6, 3.6 Hz, 1H), 4.16 (d, *J* = 8.4 Hz, 3H), 3.89 – 3.85 (m, 4H), 3.61 (s, 4H), 3.54 – 3.39 (m, 3H), 2.71 – 2.63 (m, 2H), 2.52 (s, 2H), 2.26 (s, 5H), 2.19 – 1.98 (m, 9H), 1.9(m, 1H), 1.78 – 1.67 (m, 2H), 1.56 (qd, *J* = 11.7, 4.6 Hz, 2H)

Cpd Number	^{1}H NMR data
353	(400 MHz, pyridine-d_5) δ ppm 8.37 (d, J = 8.1 Hz, 2H), 7.64 (s, 1H), 7.48 – 7.42 (m, 2H), 7.24 (t, J = 7.4 Hz, 1H), 4.26 – 4.10 (m, 7H), 3.52 – 3.43 (m, 2H), 3.27 – 3.13 (m, 2H), 2.73 – 2.62 (m, 2H), 2.57 – 2.47 (m, 2H), 2.45 – 2.37 (m, 4H), 2.33 (dt, J = 7.1, 3.8 Hz, 1H), 2.19 – 2.02 (m, 1H), 1.76 (d, J = 11.0 Hz, 4H), 1.63 (ddd, J = 42.1, 12.6, 4.3 Hz, 4H), 1.49 (p, J = 5.6 Hz, 4H), 1.34 (q, J = 6.1 Hz, 2H)
354	(400 MHz, pyridine-d_5) δ ppm 8.40 – 8.26 (m, 2H), 7.62 (s, 1H), 7.48 – 7.41 (m, 2H), 7.28 – 7.20 (m, 1H), 4.22 – 4.15 (m, 4H), 3.55 – 3.40 (m, 4H), 3.14 (s, 3H), 2.68 (dq, J = 11.1, 8.6 Hz, 2H), 2.57 – 2.47 (m, 2H), 2.2 (m, 3H), 1.82 – 1.72 (m, 2H), 1.69 – 1.51 (m, 4H), 0.88 (t, J = 7.4 Hz, 3H)
355	(400 MHz, pyridine-d_5) δ ppm 8.46 – 8.30 (m, 2H), 7.62 (s, 1H), 7.52 – 7.37 (m, 2H), 7.31 – 7.21 (m, 1H), 4.23 – 4.15 (m, 3H), 3.66 (q, J = 7.2 Hz, 3H), 3.61 – 3.54 (m, 2H), 3.46 (td, J = 11.6, 2.4 Hz, 3H), 2.76 – 2.60 (m, 2H), 2.52 (dddt, J = 12.5, 6.6, 4.4, 1.8 Hz, 2H), 2.28 – 2.02 (m, 3H), 1.79 – 1.65 (m, 4H), 1.63 – 1.51 (m, 2H), 1.26 (t, J = 7.1 Hz, 3H), 0.89 (t, J = 7.4 Hz, 3H)
356	(400 MHz, pyridine-d_5) δ ppm 8.39 – 8.30 (m, 2H), 7.65 (s, 1H), 7.46 – 7.36 (m, 2H), 7.29 – 7.19 (m, 1H), 3.45 (td, J = 11.6, 2.4 Hz, 2H), 3.03 – 2.88 (m, 2H), 2.68 (dq, J = 11.3, 8.9 Hz, 2H), 2.53 (dd, J = 8.5, 4.7 Hz, 2H), 2.20 – 2.00 (m, 4H), 1.85 – 1.69 (m, 4H), 1.56 (qd, J = 11.8, 4.4 Hz, 2H), 1.20 – 1.03 (m, 3H)

Cpd Number	^{1}H NMR data
357	(400 MHz, pyridine-d_5) δ ppm 8.48 – 8.32 (m, 2H), 7.65 (s, 1H), 7.43 (t, J = 7.8 Hz, 2H), 7.17 (t, 1H), 4.14 (d, J = 6.1 Hz, 3H), 3.56 – 3.36 (m, 4H), 2.67 (q, J = 9.9, 8.7 Hz, 2H), 2.53 (dd, J = 8.5, 4.5 Hz, 2H), 2.05 (s, 5H), 1.94 (t, J = 6.1 Hz, 2H), 1.76 (d, J = 13.7 Hz, 2H), 1.57 (dd, J = 12.8, 4.4 Hz, 2H)
358	(400 MHz, pyridine-d_5) δ ppm 8.42 (d, J = 8.3 Hz, 2H), 7.67 (s, 1H), 7.47 – 7.40 (m, 2H), 7.22 (t, J = 7.4 Hz, 1H), 4.19 (d, J = 8.3 Hz, 1H), 4.14 (d, J = 6.2 Hz, 2H), 4.09 – 4.03 (m, 2H), 3.74 (dd, J = 5.9, 3.3 Hz, 4H), 3.67 – 3.62 (m, 4H), 3.46 (td, J = 11.6, 2.3 Hz, 2H), 2.69 (dq, J = 11.4, 8.7 Hz, 2H), 2.58 – 2.48 (m, 2H), 2.18 – 2.03 (m, 2H), 1.80 – 1.73 (m, 2H), 1.65 – 1.54 (m, 2H)
359	(400 MHz, pyridine-d_5) δ ppm 8.43 – 8.34 (m, 2H), 7.65 (s, 1H), 7.46 (dd, J = 8.4, 7.2 Hz, 2H), 7.29 – 7.19 (m, 1H), 4.25 – 4.14 (m, 5H), 3.67 – 3.59 (m, 5H), 3.46 (td, J = 11.6, 2.2 Hz, 3H), 3.31 – 3.15 (m, 2H), 2.67 (dt, J = 11.1, 8.8 Hz, 2H), 2.54 (dq, J = 8.2, 3.9 Hz, 2H), 2.42 (dd, J = 5.8, 3.5 Hz, 4H), 2.20 – 2.11 (m, 1H), 2.11 – 2.04 (m, 2H), 1.79 (dd, J = 21.1, 14.0 Hz, 4H), 1.67 – 1.51 (m, 4H)
360	(400 MHz, pyridine-d_5) δ ppm 8.44 – 8.35 (m, 2H), 7.65 (s, 1H), 7.49 – 7.39 (m, 2H), 7.33 – 7.19 (m, 1H), 4.26 (d, J = 13.0 Hz, 2H), 4.22 – 4.13 (m, 1H), 4.12 (d, J = 6.2 Hz, 3H), 3.54 (s, 4H), 3.50 – 3.30 (m, 5H), 2.81 – 2.72 (m, 1H), 2.71 – 2.64 (m, 2H), 2.60 – 2.49 (m, 2H), 2.28 – 2.20 (m, 4H), 2.20 – 1.99 (m, 8H), 1.84 (dd, J = 14.0, 3.7 Hz, 2H), 1.76 (dd, J = 13.3, 3.1 Hz, 2H), 1.63 – 1.48 (m, 2H)

Cpd Number	^{1}H NMR data
361	(400 MHz, pyridine-d_5) δ ppm 8.42 – 8.33 (m, 2H), 7.63 (s, 1H), 7.45 (dd, J = 8.6, 7.3 Hz, 2H), 7.24 (d, J = 7.5 Hz, 1H), 7.23 (d, J = 16.2 Hz, 1H), 4.19 (d, J = 8.3 Hz, 1H), 4.14 (t, J = 7.1 Hz, 4H), 3.74 – 3.67 (m, 4H), 3.46 (td, J = 11.6, 2.3 Hz, 2H), 2.68 (dq, J = 11.2, 8.8 Hz, 2H), 2.59 – 2.49 (m, 2H), 2.44 – 2.36 (m, 4H), 2.16 (s, 4H), 2.13 – 1.99 (m, 2H), 1.82 – 1.71 (m, 2H), 1.56 (ddd, J = 13.3, 11.5, 4.7 Hz, 2H)
362	(400 MHz, pyridine-d_5) δ ppm 8.39 (d, J = 8.0 Hz, 2H), 7.60 (s, 1H), 7.49 – 7.43 (m, 2H), 7.25 (t, J = 7.4 Hz, 1H), 4.21 – 4.15 (m, 1H), 4.12 (s, 3H), 3.46 (td, J = 11.6, 2.2 Hz, 2H), 2.67 (dt, J = 11.3, 8.9 Hz, 2H), 2.56 – 2.47 (m, 2H), 2.09 (d, J = 8.2 Hz, 1H), 1.76 (d, J = 12.9 Hz, 2H), 1.65 (s, 10H), 1.62 – 1.51 (m, 3H)
364	(400 MHz, $CDCl_3$) δ ppm 9.94 (s, 1 H), 7.99 (d, J=7.3 Hz, 2 H), 7.60-7.52 (m, 2 H), 7.44 (s, 1 H), 7.41-7.31 (m, 1 H), 4.57 (s, 2 H), 3.97 (pent, J=8.5 Hz, 1 H), 3.75-3.65 (m, 2 H), 3.40 (s, 3 H), 3.38 (d, J=6.1 Hz, 2 H), 3.03-2.92 (m, 2 H), 2.69-2.57 (m, 2 H), 2.48-2.38 (m, 2 H), 2.16-2.01 (m, 2 H), 2.00-1.84 (m, 3 H), 1.64-1.52 (m, 2 H)
365	(500 MHz, DMSO-d_6) δ ppm 8.40 (d, J = 7.8 Hz, 2H), 7.58-7.53 (m, 2H), 7.35 (s, 1H), 7.31 (t, J = 7.4 Hz, 1H), 3.98 (tt, J = 8.4 Hz, 1H), 3.62-3.56 (m, 2H), 3.2-3.1 (m, 4H), 2.96 (s, 3H), 2.91-2.83 (m, 2H), 2.55-2.46 (m, 3H), 2.46-2.37 (m, 2H), 2.22-2.15 (m, 2H), 2.13-2.03 (m, 1H), 2.03-1.94 (m, 1H), 1.94-1.83 (m, 2H), 1.80-1.70 (m, 4H), 1.60-1.52 (m, 2H)

Cpd Number	^{1}H NMR data
366	(400 MHz, $CDCl_3$) δ ppm 8.05 (dd, *J*=8.4, 1.1 Hz, 2 H), 7.57 (t, *J*=7.9 Hz, 2 H), 7.45 (s, 1 H), 7.34 - 7.42 (m, 1 H), 4.13 - 4.19 (m, 2 H), 3.99 (t, *J*=8.3 Hz, 1 H), 3.67 - 3.80 (m, 5 H), 3.37 - 3.42 (m, 5 H), 2.92 - 3.01 (m, 2 H), 2.59 - 2.68 (m, 2 H), 2.39 - 2.48 (m, 2 H), 2.04 - 2.13 (m, 2 H), 1.96 (d, *J*=13.4 Hz, 2 H), 1.84 - 1.91 (m, 2 H), 1.55 - 1.63 (m, 2 H)
367	(400 MHz, $CDCl_3$) δ ppm (d, *J*=7.6 Hz, 2 H), 7.56 (d, *J*=8.1 Hz, 2 H), 7.46 (s, 1 H), 7.33 - 7.40 (m, 1 H), 3.93 - 4.05 (m, 1 H), 3.78 - 3.86 (m, 2 H), 3.65 - 3.76 (m, 4 H), 3.35 - 3.44 (m, 5 H), 2.96 (t, *J*=11.5 Hz, 2 H), 2.56 - 2.70 (m, 2 H), 2.39 - 2.48 (m, 2 H), 2.03 - 2.21 (m, 4 H), 1.96 (d, *J*=13.0 Hz, 2 H), 1.54 - 1.64 (m, 5 H)
368	(300 MHz, $CDCl_3$) δ ppm 7.99 - 8.21 (m, 2 H), 7.42 - 7.60 (m, 2 H), 7.33 (br. s., 1 H), 7.27 (s, 1 H), 6.44 (d, *J*=6.2 Hz, 1 H), 5.31 (s, 1 H), 3.97 (d, *J*=8.8 Hz, 1 H), 3.61 - 3.75 (m, 2 H), 3.31 - 3.46 (m, 5 H), 3.09 - 3.27 (m, 2 H), 2.85 - 3.04 (m, 5 H), 2.57 - 2.69 (m, 2 H), 2.36 - 2.50 (m, 2 H), 1.89 - 2.14 (m, 5 H), 1.52 - 1.66 (m, 2 H), 1.22 - 1.34 (m, 4 H)
369	(400 MHz, $CDCl_3$) δ ppm 10.02 (s, 1 H), 8.04 (d, J=8.1 Hz, 2 H), 7.56 (t, J=7.9, 2 H), 7.44 (s, 1 H), 7.36 (t, J=7.5, 1 H), 4.52-4.44 (m, 1 H), 4.31 (dd, J=10.3, 5.2 Hz, 1 H), 4.10 (dd, J=10.3, 7.9 Hz, 1 H), 4.05-3.93 (m, 2 H), 3.89-3.83 (m, 1 H), 3.72-3.65 (m, 2 H), 3.40 (s, 3 H), 3.37 (d, J=6.1 Hz, 2 H), 3.00-2.91 (m, 2 H), 2.68-2.50 (m, 3 H), 2.48-2.28 (m, 3 H), 2.14-2.01 (m, 2 H), 2.00-1.83 (m, 3 H), 1.63-1.50 (m, 2 H)

Cpd Number	^{1}H NMR data
370	(300 MHz, $CDCl_3$) δ ppm 7.88 (s, 2 H), 7.57 (s, 1 H), 3.69 (d, *J*=11.7 Hz, 2 H), 3.32 - 3.51 (m, 9 H), 2.91 - 3.08 (m, 2 H), 2.64 (s, 6 H), 1.95 (d, *J*=12.8 Hz, 3 H), 1.43 - 1.62 (m, 8 H)
371	(300 MHz, $CDCl_3$) δ ppm 8.02 (dd, *J*=8.6, 0.9 Hz, 2 H), 7.51 - 7.67 (m, 3 H), 7.42 (d, *J*=7.3 Hz, 1 H), 3.78 - 4.01 (m, 5 H), 3.43 (s, 3 H), 3.30 - 3.38 (m, 4 H), 3.12 (s, 1 H), 2.59 - 2.77 (m, 2 H), 2.34 - 2.51 (m, 2 H), 2.04 - 2.23 (m, 2 H)
372	(300 MHz, $CDCl_3$) δ ppm 8.00 - 8.09 (m, 2 H), 7.57 (t, *J*=7.9 Hz, 2 H), 7.45 (d, *J*=2.2 Hz, 1 H), 7.41 (s, 1 H), 7.34 - 7.39 (m, 1 H), 7.25 (d, *J*=1.5 Hz, 1 H), 6.00 (t, *J*=2.0 Hz, 1 H), 4.68 (t, *J*=6.4 Hz, 2 H), 4.13 (t, *J*=6.4 Hz, 2 H), 3.99 (t, *J*=8.4 Hz, 1 H), 3.69 (d, *J*=12.1 Hz, 2 H), 3.36 - 3.43 (m, 5 H), 2.95 (t, *J*=11.4 Hz, 2 H), 2.56 - 2.72 (m, 2 H), 2.38 - 2.51 (m, 2 H), 2.09 (s, 2 H), 1.94 (br. s., 3 H), 1.52 - 1.68 (m, 2 H)
373	^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 10.06 (s, 1 H), 8.03 (d, J=7.9 Hz, 2 H), 7.56 (t, J=7.9, 2 H), 7.43 (s, 1 H), 7.38-7.24 (m, 6 H), 5.04 (s, 2 H), 5.48-5.42 (m, 1 H), 3.97 (pent, J=8.4 Hz, 1 H), 3.81-3.71 (m, 4 H), 3.70-3.63 (m, 2 H), 3.40 (s, 3 H), 3.37 (d, J=6.4 Hz, 2 H), 2.98-2.89 (m, 2 H), 2.68-2.57 (m, 2 H), 2.47-2.37 (m, 2 H), 2.16-2.00 (m, 2 H), 1.99-1.82 (m, 3 H), 1.63-1.50 (m, 2 H)

Cpd Number	^{1}H NMR data
374	(400 MHz, pyridine-d_5) δ ppm 8.39 – 8.30 (m, 2H), 7.53 (s, 1H), 7.37 – 7.31 (m, 2H), 7.14 – 7.10 (m, 1H), 3.99 (t, J = 8.3 Hz, 1H), 3.47 (d, J = 12.4 Hz, 2H), 3.27 (s, 3H), 3.21 (d, J = 5.9 Hz, 2H), 2.72 (td, J = 12.2, 2.2 Hz, 2H), 2.65 – 2.57 (m, 2H), 2.44 – 2.31 (m, 2H), 2.02 – 1.90 (m, 4H), 1.80 (d, J = 12.8 Hz, 3H), 1.60 (s, 3H), 1.52 (dd, J = 12.1, 3.5 Hz, 2H), 0.96 – 0.85 (m, 2H)
375	(400 MHz, $CDCl_3$) δ ppm 9.95 (s, 1 H), 8.05 (d, J=7.9 Hz, 2 H), 7.55 (t, J=7.9, 2 H), 7.45 (s, 1 H), 7.35 (t, J=7.5 Hz, 1 H), 3.98 (pent, J=8.3 Hz, 1 H), 3.72-3.65 (m, 2 H), 3.46 (d, J=6.7 Hz, 2 H), 3.40 (s, 3 H), 3.37 (d, J=6.4 Hz, 2 H), 2.99-2.90 (m, 2 H), 2.68-2.57 (m, 2 H), 2.47-2.35 (m, 2 H), 2.15-2.00 (m, 2 H), 1.99-1.82 (m, 3 H), 1.63-1.50 (m, 3 H), 1.14 (d, J=6.8 Hz, 6 H)
376	(400 MHz, $CDCl_3$) δ ppm 10.18 (s, 1 H), 8.06 (d, J=8.4 Hz, 2 H), 7.56 (t, J=7.9, 2 H), 7.44 (s, 1 H), 7.35 (t, J=7.5 Hz, 1 H), 4.52 (s, 2 H), 3.98 (pent, J=8.6 Hz, 1 H), 3.75 (s, 3 H), 3.72-3.65 (m, 2 H), 3.40 (s, 3 H), 3.37 (d, J=6.2 Hz, 2 H), 2.99-2.91 (m, 2 H), 2.68-2.57 (m, 2 H), 2.47-2.37 (m, 2 H), 2.13-2.01 (m, 2 H), 1.99-1.82 (m, 3 H), 1.63-1.51 (m, 2 H)
377	(400 MHz, $CDCl_3$) δ ppm 10.01 (s, 1 H), 8.03 (d, J=8.03 Hz, 2 H), 7.56 (t, J=7.7, 2 H), 7.43 (s, 1 H), 7.39-7.28 (m, 6 H), 5.19-5.05 (m, 2 H), 4.54-4.44 (m, 1 H), 4.03-3.93 (m, 2 H), 3.84 (dd, J=12.3, 8.1 Hz, 1 H), 3.78-3.48 (m, 4 H), 3.40 (s, 3 H), 3.37 (d, J=6.4 Hz, 2 H), 3.00-2.90 (m, 2 H), 2.69-2.49 (m, 2 H), 2.47-2.29 (m, 2 H), 2.15-2.00 (m, 2 H), 1.99-1.82 (m, 3 H), 1.63-1.50 (m, 4 H)

Cpd Number	^{1}H NMR data
378	(400 MHz, $CDCl_3$) δ ppm 9.94 (s, 1 H), 7.94 - 8.02 (m, 2 H), 7.23 - 7.32 (m, 2 H), 5.31 (s, 1 H), 4.37 (br. s., 2 H), 3.37 - 3.58 (m, 5 H), 2.90 (d, *J*=11.3 Hz, 2 H), 1.75 - 2.00 (m, 4 H), 1.49 - 1.56 (m, 15 H)
379	(400 MHz, $CDCl_3$) δ ppm 9.95 (s br, 1H-NH), 8.24 (s, 1H), 7.93 - 8.07 (m, 2 H), 7.45 (s, 1 H), 7.18 - 7.34 (m, 2 H), 3.92 - 4.06 (m, 2 H), 3.66 - 3.90 (m, 4 H), 3.45 - 3.62 (m, 2 H), 3.41 (s, 3 H), 2.87 - 3.13 (m, 10 H), 2.27 - 2.70 (m, 7 H), 2.00 - 2.22 (m, 4 H), 1.88 (m, 2 H)
380	(400 MHz, $CDCl_3$) δ ppm 8.14 – 8.06 (m, 2H), 7.58 (dd, *J* = 8.5, 7.4 Hz, 2H), 7.47 (s, 1H), 7.37 (td, *J* = 7.3, 1.2 Hz, 1H), 4.00 (p, *J* = 8.4 Hz, 1H), 3.80 (dd, *J* = 6.0, 3.5 Hz, 4H), 3.69 (d, *J* = 12.3 Hz, 2H), 3.51 (dd, *J* = 5.8, 3.6 Hz, 4H), 3.00 – 2.89 (m, 2H), 2.68 – 2.55 (m, 6H), 2.51 (d, *J* = 7.1 Hz, 2H), 2.45 (m, 2H), 2.19 – 1.99 (m, 4H), 1.92 – 1.73 (m, 5H), 1.55 (qd, *J* = 12.2, 3.7 Hz, 2H)
381	(400 MHz, $CDCl_3$) δ ppm 8.01 ppm (dd, *J*=8.84, 4.55 Hz, 2H), 7.44 ppm (s, 1H), 7.25 ppm (t, *J*=8.46 Hz, 2H), 4.03-3.94 ppm (m, 1H), 3.73-3.69 ppm (m, 2H), 3.37 ppm (s, 3H), 3.3-3.24 ppm (m, 1H), 3.04 ppm (s, 6H), 2.97-2.87 ppm (m, 4H), 2.65-2.56 ppm (m, 2H), 2.52-2.36 ppm (m, 5H), 2.13-2.02 ppm (m, 4H), 1.9 ppm (s, 2H), 2.01-1.9 ppm (m, 2H), 1.73-1.61 ppm (m, 3H)
382	(HCl salt) (400 MHz, DMSO-d_6) δ ppm 12.2 (br s, 1H), 11.70 (br s, 1H), 11.4 (br s, 1H), 8.37-8.32 (m, 2H), 7.45-7.39 (m, 2H), 7.26 (s, 1H), 4.10-3.48 (m, 13H), 3.05-2.98 (m, 2H), 2.92 (s, 6H), 2.55-1.91 (m, 10H), 1.35-1.27 (m, 6H)

Cpd Number	^{1}H NMR data
383	(400 MHz, $CDCl_3$) δ ppm 8.11 – 8.02 (m, 2H), 7.57 (dd, *J* = 8.5, 7.4 Hz, 2H), 7.46 (s, 1H), 7.41 – 7.32 (m, 1H), 4.01 (p, *J* = 8.5 Hz, 1H), 3.84 – 3.75 (m, 8H), 3.73 (d, *J* = 12.4 Hz, 2H), 3.54 – 3.44 (m, 4H), 2.97 (td, *J* = 12.4, 2.3 Hz, 2H), 2.72 – 2.55 (m, 6H), 2.49 – 2.35 (m, 3H), 2.18 – 2.00 (m, 4H), 1.82 (qd, *J* = 12.1, 3.7 Hz, 2H)
384	(400 MHz, $CDCl_3$) δ ppm 8.05 (d, *J*=8.1 Hz, 2 H), 7.57 (t, *J*=7.7 Hz, 2 H), 7.45 (s, 1 H), 7.32 - 7.39 (m, 1 H), 6.57 (br. s., 1 H), 5.75 (br. s., 1 H), 4.45 (s, 2 H), 3.99 (quin, *J*=8.3 Hz, 1 H), 3.70 (d, *J*=12.2 Hz, 2 H), 3.31 - 3.46 (m, 5 H), 2.90 - 3.02 (m, 2 H), 2.55 - 2.72 (m, 2 H), 2.34 - 2.50 (m, 2 H), 2.03 - 2.18 (m, 2 H), 1.83 - 2.02 (m, 3 H), 1.47 - 1.68 (m, 2 H)
385	(300 MHz, $CDCl_3$) δ ppm 10.01 (br. s., 1 H), 8.33 (d, *J*=5.5 Hz, 1 H), 7.89 (dd, *J*=5.7, 1.7 Hz, 1 H), 7.70 (d, *J*=1.5 Hz, 1 H), 7.55 (s, 1 H), 4.06 (s, 3 H), 3.88 - 4.01 (m, 1 H), 3.70 (d, *J*=12.5 Hz, 2 H), 3.45 - 3.53 (m, 3 H), 3.43 (s, 3 H), 3.40 (d, *J*=6.2 Hz, 2 H), 3.00 (t, *J*=11.7 Hz, 2 H), 2.56 - 2.73 (m, 2 H), 2.39 - 2.52 (m, 2 H), 2.06 - 2.24 (m, 2 H), 1.83 - 2.03 (m, 2 H), 1.49 - 1.80 (m, 3 H)
386	(300 MHz, $CDCl_3$) δ ppm 8.08 (dd, *J*=8.7, 1.0 Hz, 2 H), 7.52 - 7.68 (m, 2 H), 7.47 (s, 1 H), 7.36 - 7.44 (m, 1 H), 6.32 (br. s., 1 H), 3.95 - 4.09 (m, 1 H), 3.81 - 3.91 (m, 2 H), 3.67 - 3.80 (m, 4 H), 3.44 (s, 3 H), 3.37 - 3.42 (m, 2 H), 2.91 - 3.07 (m, 2 H), 2.58 - 2.75 (m, 2 H), 2.33 - 2.54 (m, 2 H), 2.05 - 2.20 (m, 2 H), 2.02 (s, 3 H), 1.97 (br. s., 1 H), 1.51 - 1.82 (m, 5 H)

Cpd Number	^{1}H NMR data
387	(400 MHz, $CDCl_3$) δ ppm 8.20 (dd, *J*=8.7, 1.1 Hz, 1 H), 8.12 (dd, *J*=8.7, 1.1 Hz, 1 H), 7.45 - 7.61 (m, 2 H), 7.29 - 7.34 (m, 2 H), 3.95 - 4.25 (m, 4 H), 3.80 - 3.90 (m, 1 H), 3.71 - 3.79 (m, 4 H), 3.42 (s, 3 H), 3.38 (d, *J*=6.4 Hz, 2 H), 2.84 - 2.96 (m, 2 H), 2.64 (quin, *J*=9.4 Hz, 2 H), 2.36 - 2.49 (m, 4 H), 2.02 - 2.15 (m, 2 H), 1.95 (d, *J*=13.2 Hz, 2 H), 1.82 - 1.91 (m, 4 H)
388	(400 MHz, pyridine-d_5) δ ppm 8.39 – 8.32 (m, 2H), 7.57 (s, 1H), 7.41 – 7.32 (m, 2H), 7.17 (d, *J* = 1.2 Hz, 1H), 4.23 (dd, *J* = 26.9, 12.9 Hz, 2H), 4.00 (t, *J* = 8.3 Hz, 1H), 3.57 – 3.45 (m, 2H), 3.27 (m, 7H), 3.26 – 3.13 (m, 5H), 2.80 – 2.70 (m, 4H), 2.63 (m, 2H), 2.08 – 1.86 (m, 14H), 1.72 (m, 2H)
389	(400 MHz, pyridine-d_5) δ ppm 8.42 – 8.30 (m, 2H), 7.56 (s, 1H), 7.37 (dd, *J* = 8.6, 7.3 Hz, 2H), 5.7 (m, 1H), 4.28-3.99 (m, 9H), 3.21 (d, *J* = 5.9 Hz, 5H), 2.90 – 2.62 (m, 11H), 2.12 (s, 3H), 1.9 (m, 10H), 1.61 – 1.42 (m, 2H)
390	(400 MHz, pyridine-d_5) δ ppm 8.39 – 8.31 (m, 2H), 7.57 (s, 1H), 7.41 – 7.32 (m, 2H), 7.17 (d, *J* = 1.1 Hz, 1H), 4.33 – 4.16 (m, 2H), 4.00 (p, *J* = 8.3 Hz, 1H), 3.61 – 3.46 (m, 3H), 3.30 – 3.12 (m, 13H), 2.80 – 2.56 (m, 5H), 2.46 – 2.31 (m, 2H), 1.96 (td, *J* = 12.3, 10.7, 6.1 Hz, 3H), 1.85 – 1.63 (m, 10H), 1.62 – 1.47 (m, 3H)
391	(400 MHz, pyridine-d_5) δ ppm 8.44 – 8.30 (m, 2H), 7.55 (s, 1H), 7.40 – 7.25 (m, 2H), 7.31 (s, 2H), 7.16 (d, *J* = 1.2 Hz, 1H), 4.73 (dd, *J* = 6.2, 4.9 Hz, 1H), 4.14 – 3.84 (m, 2H), 3.52 – 3.41 (m, 4H), 3.23 (d, *J* = 25.0 Hz, 6H), 3.10 (s, 3H), 2.79 – 2.56 (m, 5H), 2.44 – 2.31 (m, 2H), 2.04 – 1.90 (m, 2H), 1.80 (d, *J* = 12.6 Hz, 3H), 1.61 – 1.45 (m, 4H), 0.77 (t, *J* = 7.4 Hz, 3H)

Cpd Number	^{1}H NMR data
392	(400 MHz, pyridine-d_5) δ ppm 8.43 – 8.31 (m, 2H), 7.55 (s, 1H), 7.40 – 7.29 (m, 2H), 7.17 (d, J = 1.1 Hz, 1H), 3.99 (t, J = 8.3 Hz, 1H), 3.69 – 3.52 (m, 4H), 3.47 (d, J = 12.3 Hz, 2H), 3.26 (s, 3H), 3.20 (d, 1H), 2.77 – 2.56 (m, 4H), 2.43 – 2.30 (m, 2H), 2.04 – 1.91 (m, 2H), 1.83 – 1.69 (m, 3H), 1.69 – 1.48 (m, 4H), 1.18 (t, J = 7.1 Hz, 3H), 0.78 (t, J = 7.4 Hz, 3H)
393	(400 MHz, pyridine-d_5) δ ppm 8.41 – 8.33 (m, 2H), 7.57 (s, 1H), 7.40 – 7.31 (m, 2H), 7.16 (d, J = 1.2 Hz, 1H), 4.10 – 3.88 (m, 5H), 3.43 (d, J = 12.2 Hz, 2H), 3.26 (s, 3H), 3.20 (d, J = 5.9 Hz, 2H), 2.79 (ddd, J = 14.0, 11.7, 2.8 Hz, 2H), 2.73 – 2.56 (m, 4H), 2.36 (ddd, J = 11.6, 8.4, 5.5 Hz, 2H), 2.21 (dd, J = 13.0, 3.9 Hz, 2H), 1.77 (d, J = 12.2 Hz, 5H), 1.03 (t, J = 7.1 Hz, 3H)
394	(400 MHz, pyridine-d_5) δ ppm 8.35 (dt, J = 8.7, 1.1 Hz, 2H), 7.56 (d, J = 9.8 Hz, 1H), 7.34 (ddd, J = 7.4, 5.4, 3.6 Hz, 2H), 4.06 – 3.92 (m, 1H), 3.90 (d, J = 5.8 Hz, 1H), 3.85 (dd, J = 6.7, 4.2 Hz, 1H), 3.83 – 3.72 (m, 2H), 3.68 (t, J = 6.0 Hz, 1H), 3.65 – 3.60 (m, 1H), 3.57 – 3.45 (m, 3H), 3.35 (t, J = 6.3 Hz, 1H), 3.26 (s, 3H), 3.21 (d, J = 5.9 Hz, 2H), 2.74 (t, J = 12.5 Hz, 2H), 2.69 – 2.56 (m, 2H), 2.38 (d, J = 8.2 Hz, 2H), 2.04 (m, 1H), 1.98 (d, J = 10.6 Hz, 4H), 1.87 – 1.66 (m, 5H), 1.59 – 1.46 (m, 2H)

Cpd Number	^{1}H NMR data
395	(400 MHz, pyridine-d_5) δ ppm 8.39 – 8.32 (m, 2H), 7.57 (s, 1H), 7.41 – 7.32 (m, 2H), 7.17 (d, J = 1.2 Hz, 1H), 4.23 (dd, J = 26.9, 12.9 Hz, 2H), 4.00 (t, J = 8.3 Hz, 1H), 3.57 – 3.45 (m, 3H), 3.27 (s, 3H), 3.26 – 3.13 (m, 9H), 3.08 (d, J = 11.8 Hz, 1H), 2.99 (m, 1H), 2.80 – 2.70 (m, 2H), 2.63 (pd, J = 9.0, 2.5 Hz, 3H), 2.37 (ttd, J = 8.6, 6.1, 2.5 Hz, 2H), 2.08 – 1.86 (m, 4H), 1.85 – 1.73 (m, 6H), 1.72 (m, 2H), 1.62 – 1.46 (m, 3H)
396	(400 MHz, pyridine-d_5) δ ppm 8.36 (d, J = 8.0 Hz, 2H), 7.57 (s, 1H), 7.45 – 7.26 (m, 2H), 7.30 (m, 1H), 4.00 (p, J = 8.3 Hz, 1H), 3.72 – 3.60 (m, 9H), 3.50 (d, J = 12.2 Hz, 2H), 3.27 (s, 3H), 3.22 (d, J = 5.9 Hz, 2H), 2.82 – 2.70 (m, 2H), 2.66 – 2.54 (m, 2H), 2.46 – 2.30 (m, 2H), 2.03 – 1.90 (m, 2H), 1.81 (d, J = 12.0 Hz, 4H), 1.53 (d, J = 12.5 Hz, 2H)
397	(400 MHz, pyridine-d_5) δ ppm 8.42 – 8.30 (m, 2H), 7.57 (s, 1H), 7.39 (d, J = 1.9 Hz, 2H), 7.15 (d, J = 1.5 Hz, 1H), 4.32 – 4.22 (m, 1H), 3.99 (t, J = 8.3 Hz, 1H), 3.64 – 3.49 (m, 5H), 3.47 (d, 1H), 3.27 (s, 3H), 3.23 – 3.13 (m, 5H), 2.76 (d, J = 2.1 Hz, 1H), 2.74 – 2.63 (m, 2H), 2.39 (dq, J = 6.3, 3.1 Hz, 5H), 2.34 (d, J = 2.5 Hz, 1H), 2.24 (tt, J = 10.9, 3.6 Hz, 1H), 2.10 – 1.99 (m, 1H), 1.78 (ddd, J = 21.4, 11.5, 3.5 Hz, 5H), 1.69 – 1.49 (m, 4H)
398	(400 MHz, pyridine-d_5) δ ppm 8.42 – 8.30 (m, 2H), 7.56 (s, 1H), 7.37 (dd, J = 8.6, 7.3 Hz, 2H), 4.28 (d, J = 9.3 Hz, 1H), 3.99 (t, J = 8.3 Hz, 1H), 3.64 (s, 2H), 3.46 (t, J = 11.7 Hz, 5H), 3.35 (dd, J = 12.4, 2.6 Hz, 1H), 3.27 (s, 3H), 3.21 (d, J = 5.9 Hz, 2H), 2.90 – 2.62 (m, 4H), 2.30 (s, 4H), 2.21 (s, 1H), 2.12 (s, 4H), 2.05 – 1.97 (m, 1H), 1.79 (d, J = 6.5 Hz, 6H), 1.61 – 1.42 (m, 2H)

Cpd Number	^{1}H NMR data
399	(400 MHz, pyridine-d_5) δ ppm 8.35 (d, J = 8.0 Hz, 3H), 7.54 (s, 2H), 7.41 – 7.32 (m, 3H), 4.75 (s, 1H), 4.63 (q, J = 4.5 Hz, 1H), 3.99 (t, J = 8.3 Hz, 1H), 3.75 (q, J = 5.4, 5.0 Hz, 6H), 3.48 (d, J = 12.2 Hz, 3H), 3.27 (s, 4H), 3.21 (d, J = 5.9 Hz, 3H), 2.80 – 2.67 (m, 3H), 2.66 – 2.54 (m, 2H), 2.37 (ddt, J = 8.4, 6.0, 2.5 Hz, 3H), 1.97 (td, J = 9.2, 4.4 Hz, 3H), 1.88 – 1.71 (m, 8H), 1.57 – 1.42 (m, 3H)
400	(400 MHz, pyridine-d_5) δ ppm 8.45 – 8.37 (m, 2H), 7.61 (s, 1H), 7.46 – 7.37 (m, 2H), 4.06 (p, J = 8.3 Hz, 1H), 3.87 – 3.75 (m, 4H), 3.55 (d, J = 12.2 Hz, 2H), 3.34 (s, 3H), 3.28 (d, J = 5.9 Hz, 2H), 2.80 (td, J = 12.2, 2.2 Hz, 2H), 2.70 (td, J = 8.9, 2.6 Hz, 2H), 2.52 – 2.37 (m, 6H), 2.18 (s, 3H), 2.04 (td, J = 9.2, 5.0 Hz, 2H), 1.89 – 1.71 (m, 2H), 1.64 – 1.49 (m, 2H)
401	(400 MHz, pyridine-d_5) δ ppm 8.37 – 8.29 (m, 2H), 7.58 (s, 1H), 7.31 (dd, J = 7.0, 1.6 Hz, 2H), 7.14 – 7.07 (m, 1H), 3.99 (p, J = 8.3 Hz, 1H), 3.67 – 3.49 (m, 1H), 3.27 (s, 3H), 3.21 (d, J = 5.9 Hz, 2H), 2.74 (s, 1H), 2.73 – 2.63 (m, 2H), 2.49 – 2.35 (m, 1H), 1.98 (dd, J = 9.1, 6.1 Hz, 1H), 1.92 – 1.75 (m, 3H), 1.69 – 1.45 (m, 3H), 1.06 – 0.91 (m, 2H)
402	(400 MHz, pyridine-d_5) δ ppm 8.44 – 8.30 (m, 2H), 7.55 (s, 1H), 7.40 – 7.25 (m, 2H), 7.31 (s, 2H), 7.16 (m, 1H), 4.73 (m, 1H), 4.14 – 3.84 (m, 2H), 3.52 – 3.41 (S, 3H), 3.23 (d, J = 25.0 Hz, 2H), 3.10 (s, 6H), 2.44 – 2.31 (m, 2H), 2.04 – 1.90 (m, 2H), 1.80 (d, J = 12.6 Hz, 4H), 1.61 – 1.45 (m, 2H)

Cpd Number	^{1}H NMR data
403	(400 MHz, pyridine-d_5) δ ppm 8.33 (d, J = 1.3 Hz, 2H), 7.58 (s, 1H), 7.31 (m, J = 2.0 Hz, 2H), 7.14 – 7.07 (m, 1H), 4.01 (m, 1H), 3.85 (m, 1H), 3.51 (d, J = 24.0 Hz, 2H), 3.27 (s, 4H), 2.75 (d, J = 2.0 Hz, 1H), 2.71 – 2.60 (m, 3H), 2.37 (td, J = 5.7, 2.4 Hz, 2H), 1.99 (d, J = 6.2 Hz, 2H), 1.94 – 1.72 (m, 4H), 1.64 – 1.51 (m, 2H), 1.35 (s, 3H)
404	(400 MHz, $CDCl_3$) δ ppm 13.56 (br s, 1H-NH), 10.15 (s, 1H-NH), 7.89 (s, 1H), 7.80 (s, 4H), 5.06 (septet, 1H), 4.76-4.83 (m, 1H), 4.36 (t, 2H), 4.23 (d, 2H); 3.99 (dd, 2H), 3.48 (s, 1H), 3.47 (s, 3H), 3.36 (d, 2H), 2.85-2.94 (m, 2H), 1.92-2.05 (m, 6H), 1.77-1.84 (m, 2H), 1.35-1.40 (m, 1H), 1.31 (d, 6H)
405	(400 MHz, $CDCl_3$) δ ppm 13.51 (br s, 1H-NH), 10.09 (s, 1H-NH), 7.88 (s, 1H), 7.82 (s, 4H), 5.07 (septet, 1H), 4.78-4.83 (m, 1H), 4.34 (t, 2H), 4.24 (d, 2H); 3.98 (dd, 2H), 3.91-3.95 (m, 2H), 3.82-3.86 (m, 2H), 3.38 (d, 2H), 3.32 (s, 3H), 2.86-2.95 (m, 2H), 1.94-2.06 (m, 6H), 1.79-1.83 (m, 1H), 1.54-1.60 (m, 2H), 1.32 (d, 6H)
406	(400 MHz, $CDCl_3$) δ ppm 13.44 (br s, 1H-NH), 10.00 (s, 1H-NH), 7.81 (s, 1H), 7.74 (s, 4H), 5.01 (septet, 1H), 4.73-4.77 (m, 1H), 4.25 (t, 2H), 4.17 (d, 2H); 3.88 (dd, 1H), 3.63 (s+m, 6+1H), 3.42 (s, 1H), 3.29 (d, 2H), 3.02 (s, 4H), 2.74-2.87 (m, 2H), 1.87-1.97 (m, 4H), 1.72-1.75 (m, 1H), 1.24 (d, 6H)

Cpd Number	^{1}H NMR data
407	(400 MHz, $CDCl_3$) δ ppm 13.30 (br s, 1H-NH), 9.86 (br s, 1H-NH), 7.90-7.94 (m, 2H), 7.36 (s, 1H), 7.15-7.20 (m, 2H), 4.37 (t, 2H), 3.98 (d, 2H), 3.67-3.88 (m, 7H), 3.57-3.61 (m, 1H), 3.44-3.47 (m, 2H), 3.23-3.24 (m, 1H), 3.17 (s, 3H), 2.92-3.02 (m, 4H), 2.48-2.55 (m, 2H), 2.36-2.40 (m, 4H), 2.22-2.24 (m, 2H)
410	(400 MHz, $CDCl_3$) δ ppm 12.95 (br s, 1H-NH), 9.96 (br s, 1H-NH), 7.93-7.98 (m, 2H), 7.40 (s, 1H), 7.19-7.25 (m, 2H), 4.44 (t, 2H), 3.98 (d, 2H), 3.86-3.94 (m, 1H), 3.66 (d, 2H), 3.51-3.58 (m, 2H), 3.39 (s, 3H), 2.89-3.05 (m, 6H), 2.49-2.61 (m, 2H), 2.36-2.46 (m, 2H), 2.22-2.34 (m, 3H), 1.98-2.14 (m, 2H), 1.66-1.79 (m, 2H)
411	(400 MHz, DMSO-d_6) δ ppm 8.37-8.31 (m, 2H), 7.40 (dd, J = 9.1, 8.6 Hz, 2H), 7.36 (s, 1H), 3.71-3.63 (m, 6H), 3.51-3.41 (m, 1H), 3.24 (s, 3H), 2.99-2.90 (m, 2H), 2.80-2.73 (m, 4H), 2.73-2.64 (m, 1H), 2.13-2.05 (m, 2H), 1.75-1.63 (m, 2H), 1.43 (d, J = 6.7 Hz, 6H)
412	(400 MHz, DMSO-d_6) δ ppm 8.36-8.30 (m, 2H), 7.40 (dd, J = 9.1, 8.6 Hz, 2H), 7.31 (s, 1H), 3.69-3.60 (m, 6H), 3.47 (hept, J = 6.7 Hz, 1H), 3.00-2.91 (m, 2H), 2.89 (s, 6H), 2.63-2.57 (m, 4H), 2.50-2.43 (m, 1H), 2.07-2.00 (m, 2H), 1.71-1.59 (m, 2H), 1.42 (d, J = 6.7 Hz, 6H)
413	(501 MHz, $CDCl_3$) δ ppm 7.99-7.94 (m, 2H), 7.52 (s, 1H), 7.27-7.22 (m, 2H), 3.80-3.76 (m, 4H), 3.76-3.70 (m, 2H), 3.59 (q, J = 7.4 Hz, 2H), 3.47 (hept, J = 6.8 Hz, 1H), 3.01-2.94 (m, 2H), 2.67-2.62 (m, 4H), 2.45-2.38 (m, 1H), 2.13-2.07 (m, 2H), 1.83-1.74 (m, 2H), 1.46 (d, J = 6.8 Hz, 6H), 1.44 (d, J = 7.4 Hz, 3H)

Cpd Number	^{1}H NMR data
414	(400 MHz, $CDCl_3$) δ ppm 8.00-7.94 (m, 2H), 7.54 (s, 1H), 7.28-7.21 (m, 2H), 3.81-3.76 (m, 4H), 3.76-3.70 (m, 2H), 3.52-3.41 (m, 1H), 3.07-2.93 (m, 3H), 2.67-2.62 (m, 4H), 2.47-2.36 (m, 1H), 2.14-2.06 (m, 2H), 1.85-1.73 (m, 2H), 1.53-1.48 (m, 2H), 1.46 (d, J = 6.8 Hz, 6H), 1.18-1.11 (m, 2H)
415	(400 MHz, $CDCl_3$) δ ppm 13.35 ppm (s, 1H), 9.93 ppm (s, 1H), 8.01 ppm (dd, J=7.58, 4.55 Hz, 2H), 7.44 ppm (s, 1H), 7.24 ppm (d, J=4.55 Hz, 2H), 4.37 ppm (t, J=12.13 Hz, 2H), 4.01 ppm (d, J=12.13 Hz, 2H), 3.94 ppm (t, J=8.34 Hz, 1H), 3.89-3.86 ppm (m, 2H), 3.79-3.76 ppm (m, 2H), 3.71-3.66 ppm (m, 3H), 3.49 ppm (d, J=11.12 Hz, 2H), 3.26 ppm (s, 3H), 3.11-3.05 ppm (m, 2H), 2.99-2.86 ppm (m, 4H), 2.66-2.56 ppm (m, 2H), 2.46-2.38 ppm (m, 2H), 2.15-2.03 ppm (m, 4H), 1.93 ppm (d, J=11.12 Hz, 2H), 1.75-1.6 ppm (m, 3H)
416	(300 MHz, $CDCl_3$) δ ppm 7.87 (dd, *J*=9.0, 4.6 Hz, 2 H), 7.27 - 7.45 (m, 1 H), 7.04 - 7.25 (m, 2 H), 3.95 (br. s., 1 H), 3.66 - 3.90 (m, 3 H), 3.55 (br. s., 1 H), 3.34 (s, 3 H), 2.95 (br. s., 2 H), 2.81 (br. s., 1 H), 2.43 - 2.65 (m, 4 H), 2.39 (br. s., 4 H), 2.20 (s, 1 H), 1.89 - 2.15 (m, 5 H), 1.74 (d, *J*=9.9 Hz, 1 H), 1.55 (d, *J*=19.4 Hz, 2 H)

Cpd Number	^{1}H NMR data
419	(400 MHz, $CDCl_3$) δ ppm, 13.55 ppm (s, 1H), 10.08 ppm (s, 1H), 7.33 ppm (s, 1H), 4.83-4.76 ppm (m, 1H), 4.47 ppm (t, J=11.87 Hz, 2H), 4.05 ppm (d, J=11.12 Hz, 2H), 3.92-3.9 ppm (m, 2H), 3.86-3.77 ppm (m, 6H), 3.67-3.63 ppm (m, 1H), 3.47 ppm (d, J=12.13 Hz, 2H), 3.32 ppm (s, 3H), 3.27-3.2 ppm (m, 1H), 3.09-3.02 ppm (m, 2H), 2.94 ppm (t, J=11.37 Hz, 2H), 2.58-2.35 ppm (m, 6H), 2.29-2.2 ppm (m, 2H), 2.14-2.03 ppm (m, 4H), 1.96 ppm (d, J=10.61 Hz, 4H), 1.81 ppm (d, J=13.64 Hz, 1H), 1.62-1.53 ppm (m, 2H), 1.43-1.33 ppm (m, 1H)
420	(400 MHz, $CDCl_3$) δ ppm, 13.5 ppm (s, 1H), 10.06 ppm (s, 1H), 7.33 ppm (s, 1H), 4.83-4.76 ppm (m, 1H), 4.54-4.43 ppm (m, 2H), 4.11-4.01 ppm (m, 2H), 3.87-3.73 ppm (m, 4H), 3.71-3.63 ppm (m, 1H), 3.53-3.44 ppm (m, 2H), 3.11-3.03 ppm (m, 8H), 2.99-2.9 ppm (m, 2H), 2.59-2.34 ppm (m, 7H), 2.29-2.2 ppm (m, 2H), 2.14-2.02 ppm (m, 4H), 1.96 ppm (d, J=11.12 Hz, 5H), 1.81 ppm (d, J=12.63 Hz, 1H), 1.67-1.51 ppm (m, 2H), 1.42-1.34 ppm (m, 2H)
421	(400 MHz, $CDCl_3$) δ ppm 9.94 (br. s, 1 H), 7.96 – 8.00 (m, 2 H), 7.47 (s, 1 H), 7.26 – 7.31 (m, 2 H), 4.45 – 4.51 (t, 2 H), 4.06 – 4.10 (m., 2 H), 3.92 – 3.97 (m, 1 H), 3.83 – 3.87 (m., 2 H), 3.50 – 3.56 (m, 2 H), 3.43 (s, 3 H), 3.22 – 3.31 (m, 1 H), 3.00 – 3.11 (m, 4 H), 2.56 – 2.67 (m, 2 H), 2.45 – 2.52 (m, 4 H), 2.28 – 2.37 (m, 2 H), 2.06 – 2.21 (m, 2 H)
422	(400 MHz, $CDCl_3$) δ ppm 13.28 (br s, 1H-NH), 10.16 (br s, 1H-NH), 7.90 (s, 1H), 7.80 (d, 2H), 7.55 (d, 2H), 5.10 (septet, 1H), 4.77-4.80 (m, 1H), 3.75-4.21 (m, 2H), 3.51-3.60 (m, 2H), 3.46 (s, 3H), 2.86 (br s, 5H), 1.94-2.18 (m, 9H), 1.78-1.82 (m, 1H), 1.56-1.59 (m, 2H), 1.31 (d, 6H)

Cpd Number	^{1}H NMR data
423	(400 MHz, $CDCl_3$) δ ppm 13.29 (br s, 1H-NH), 10.07 (br s, 1H-NH), 7.88 (s, 1H), 7.80 (d, 2H), 7.53 (d, 2H), 5.07 (septet, 1H), 4.78-4.83 (m, 1H), 3.49-3.53 (m, 2H), 3.08 (s, 6H), 2.86 (br s, 5H), 1.93-2.15 (m, 9H), 1.77-1.81 (m, 1H), 1.54-1.63 (m, 2H), 1.34-1.38 (m, 1H), 1.30 (d, 6H)
424	(400 MHz, $CDCl_3$) δ ppm, 13.26 ppm (s, 1H), 10.12 ppm (s, 1H), 7.31 ppm (s, 1H), 4.81-4.75 ppm (m, 1H), 4.35 ppm (t, J=12.13 Hz, 2H), 4.0 ppm (d, J=10.61 Hz, 2H), 3.89-3.76 ppm (m, 2H), 3.62 ppm (d, J=10.61 Hz, 3H), 3.48 ppm (d, J=11.12 Hz, 2H), 3.07 ppm (s, 8H), 2.92-2.81 ppm (m, 5H), 2.57-2.49 ppm (m, 2H), 2.37-2.31 ppm (m, 2H), 2.13-1.78 ppm (m, 16H), 1.71-1.49 ppm (m, 9H), 1.42-1.32 ppm (m, 1H)
426	(400 MHz, DMSO-d_6, 90 °C) δ ppm 8.33-8.28 (m, 2H), 7.56-7.51 (m, 2H), 7.34-7.28 (m, 2H), 4.01 (p, J = 8.1 Hz, 1H), 3.66-3.60 (m, 2H), 3.01-2.93 (m, 2H), 2.85 (s, 6H), 2.74-2.69 (m, 4H), 2.56-2.41 (m, 5H), 2.11-1.98 (m, 4H), 1.83-1.72 (m, 2H), 1.64-1.57 (m, 4H), 1.50-1.43 (m, 2H)
427	(400 MHz, DMSO-d_6, 90 °C) δ ppm 8.36-8.32 (m, 2H), 7.56-7.50 (m, 2H), 7.33-7.28 (m, 2H), 4.00 (p, J = 8.2 Hz, 1H), 3.66-3.58 (m, 2H), 3.34-3.27 (m, 2H), 2.99-2.91 (m, 2H), 2.90-2.85 (m, 4H), 2.56-2.40 (m, 5H), 2.12-1.98 (m, 4H), 1.88-1.76 (m, 2H), 1.71-1.62 (m, 4H), 1.54-1.47 (m, 2H), 1.24 (t, J = 7.4 Hz, 3H)
428	(400 MHz, DMSO-*d6*, 90 °C) δ ppm 8.32 (d, J = 8.1 Hz, 2H), 7.56-7.49 (m, 2H), 7.34-7.27 (m, 2H), 4.00 (p, J = 8.1 Hz, 1H), 3.66-3.58 (m, 2H), 3.04-2.91 (m, 3H), 2.88-2.83 (m, 4H), 2.56-2.40 (m, 5H), 2.12-1.96 (m, 4H), 1.87-1.75 (m, 2H), 1.70-1.61 (m, 4H), 1.54-1.46 (m, 2H), 1.12-1.06 (m, 2H), 0.97-0.89 (m, 2H)

Cpd Number	^{1}H NMR data
431	(400 MHz, $CDCl_3$) δ ppm 7.87 - 8.06 (m, 2 H), 7.46 (s, 1 H), 7.17 - 7.34 (m, 2 H), 4.37 (t, *J*=12.0 Hz, 2 H), 3.87 - 4.07 (m, 3 H), 3.69 (d, *J*=12.4 Hz, 2 H), 3.47 - 3.56 (m, 2 H), 3.43 (s, 3 H), 3.14 (s, 3 H), 3.05 - 3.13 (m, 2 H), 2.83 - 3.05 (m, 4 H), 2.55 - 2.70 (m, 2 H), 2.43 (q, *J*=8.3 Hz, 2 H), 2.02 - 2.18 (m, 4 H), 1.95 (d, *J*=11.3 Hz, 2 H)
432	(400 MHz, pyridine-d_5) δ ppm 8.43 – 8.30 (m, 2H), 7.58 (s, 1H), 7.37 (d, *J* = 2.0 Hz, 2H), 4.02 (m, 1H), 3.54 (d, *J* = 12.5 Hz, 2H), 3.48 (dd, *J* = 8.1, 6.5 Hz, 2H), 3.10 (s, 3H), 2.79 (t, *J* = 11.7 Hz, 2H), 2.81 – 2.68 (m, 2H), 2.59 (d, *J* = 19.2 Hz, 1H), 2.55 (d, *J* = 4.6 Hz, 4H), 2.43 (d, *J* = 8.7 Hz, 3H), 2.06 – 1.89 (m, 4H), 1.75 (q, *J* = 11.7, 11.1 Hz, 2H), 1.54 (d, *J* = 7.3 Hz, 1H), 0.77 (t, *J* = 7.3 Hz, 3H)
433	(400 MHz, pyridine-d_5) δ ppm 8.41 – 8.33 (m, 2H), 7.59 (s, 1H), 7.40 – 7.31 (m, 2H), 7.17 (d, *J* = 1.2 Hz, 1H), 4.12 – 3.87 (m, 5H), 3.77 (t, *J* = 4.5 Hz, 4H), 3.50 (d, *J* = 12.3 Hz, 2H), 2.86 – 2.56 (m, 10H), 2.49 – 2.35 (m, 3H), 2.21 (dd, *J* = 12.8, 3.8 Hz, 2H), 2.00 (ddd, *J* = 20.2, 15.9, 9.7 Hz, 4H), 1.84 – 1.70 (m, 4H), 1.05 (t, 3H)
434	(400 MHz, pyridine-d_5) δ ppm 8.39 – 8.31 (m, 2H), 7.57 (s, 1H), 7.40 – 7.31 (m, 2H), 7.17 (t, *J* = 1.2 Hz, 1H), 4.69 (dt, *J* = 47.2, 4.0 Hz, 1H), 4.03 (p, *J* = 8.3 Hz, 1H), 3.76 (q, *J* = 5.3, 4.9 Hz, 8H), 3.54 (d, *J* = 12.5 Hz, 2H), 2.84 – 2.73 (m, 2H), 2.66 (td, *J* = 8.9, 2.6 Hz, 2H), 2.57 (t, *J* = 4.6 Hz, 4H), 2.49 – 2.30 (m, 3H), 1.99 (dtd, *J* = 13.1, 10.3, 9.8, 6.8 Hz, 4H), 1.82 (tdt, *J* = 23.7, 11.4, 6.6 Hz, 6H)

Cpd Number	^{1}H NMR data
435	(400 MHz, pyridine-d_5) δ ppm 8.39 – 8.31 (m, 2H), 7.57 (s, 1H), 7.39 – 7.28 (m, 2H), 7.12 (t, *J* = 1.2 Hz, 1H), 4.01 (q, *J* = 8.3 Hz, 1H), 3.75 (t, *J* = 4.6 Hz, 4H), 3.53 (d, *J* = 12.5 Hz, 2H), 2.78 (dd, *J* = 12.8, 10.5 Hz, 2H), 2.66 (dq, *J* = 11.7, 9.1 Hz, 2H), 2.55 (t, *J* = 4.6 Hz, 4H), 2.42 (ddd, *J* = 8.2, 5.8, 3.5 Hz, 2H), 2.37 – 2.26 (m, 1H), 2.07 – 1.91 (m, 6H), 1.82 – 1.68 (m, 2H), 1.60 (s, 3H), 0.95 – 0.87 (m, 2H)
436	(400 MHz, pyridine-d_5) δ ppm 8.37 – 8.29 (m, 2H), 7.60 (s, 1H), 7.33 – 7.26 (m, 2H), 7.13 – 7.07 (m, 1H), 4.02 (t, *J* = 8.3 Hz, 1H), 3.78 (t, *J* = 4.6 Hz, 4H), 3.52 (ddd, *J* = 12.8, 8.8, 4.0 Hz, 3H), 2.78 (td, *J* = 12.3, 2.3 Hz, 2H), 2.72 – 2.57 (m, 6H), 2.48 – 2.34 (m, 3H), 2.05 – 1.93 (m, 4H), 1.79 (qd, *J* = 11.7, 3.6 Hz, 2H), 1.50 – 1.40 (m, 2H), 1.05 – 0.93 (m, 2H)
437	(501 MHz, DMSO-d_6) δ ppm 1.16 (t, J = 7.3 Hz, 2H), 1.19 1.27 (m, 3H), 1.64 1.79 (m, 2H), 1.89 2.02 (m, 1H), 2.02 2.15 (m, 3H), 2.34 2.46 (m, 2H), 2.68 (s, 1H), 2.77 (s, 4H), 2.87 3.00 (m, 2H), 3.08 (q, J = 7.3 Hz, 1H), 3.44 (q, J = 7.4 Hz, 2H), 3.61 (d, J = 12.4 Hz, 3H), 3.67 (t, J = 4.6 Hz, 4H), 3.89 4.04 (m, 1H), 7.25 (s, 1H), 7.30 7.38 (m, 1H), 7.51 7.60 (m, 2H), 8.28 8.38 (m, 2H)
438	(400 MHz, pyridine-d_5) δ ppm 8.36 – 8.29 (m, 2H), 7.57 (s, 1H), 7.34 – 7.25 (m, 2H), 7.13 – 7.06 (m, 1H), 4.20 (t, *J* = 5.8 Hz, 2H), 3.90 (t, *J* = 5.8 Hz, 2H), 3.79 (t, *J* = 4.6 Hz, 4H), 3.51 (d, *J* = 12.3 Hz, 2H), 3.09 (s, 3H), 2.81 – 2.67 (m, 3H), 2.64 (dt, *J* = 5.0, 2.7 Hz, 5H), 2.42 (tdd, *J* = 11.6, 7.3, 3.8 Hz, 3H), 2.06 – 1.94 (m, 4H), 1.81 (tt, *J* = 12.2, 6.2 Hz, 2H)

Cpd Number	^{1}H NMR data
439	(400 MHz, pyridine-d_5) δ ppm 8.39 – 8.32 (m, 2H), 7.60 (s, 1H), 7.51 – 7.38 (m, 2H), 7.31 (d, 1H), 7.18 (s, 1H), 4.27 (d, J = 12.7 Hz, 1H), 4.03 (t, J = 8.3 Hz, 1H), 3.76 (t, J = 4.6 Hz, 4H), 3.56 (d, J = 12.8 Hz, 3H), 3.41 – 3.07 (m, 8H), 2.80 (t, J = 11.7 Hz, 2H), 2.77 – 2.55 (m, 7H), 2.54 – 2.34 (m, 3H), 1.99 (dd, J = 18.7, 10.7 Hz, 5H), 1.93 – 1.57 (m, 8H)
440	(400 MHz, $CDCl_3$) δ ppm 13.0 (br s, 1H), 9.91 (br s, 0.5H), 9.50 (br s, 0.5H), 8.00-7.98 (m, 2H), 7.44 (s, 1H), 7.28-7.21 (m, 2H), 4.60-4.49 (m, 2H), 4.07-3.97 (m, 2H), 3.96-3.88 (m, 1H), 3.79-3.72 (m, 1H), 3.69-3.40 (m, 4H), 3.20-3.13 (m, 1H), 3.07-2.96 (m, 9H), 2.66-2.39 (m, 5H), 2.22-2.02 (m, 3H), 2.00-1.72 (m, 3H), 1.53-1.48 (m,3H)
441	(400 MHz, $CDCl_3$) δ ppm 13.45 (br s, 1H-NH), 12.99 (br s, 1H-NH), 10.19 (br s, 1H-NH), 7.74-7.83 (d, 5H), 4.99-5.02 (m, 1H), 4.75-4.80 (m, 1H), 4.48 (br s, 2H), 4.01-4.20 (m, 5H), 3.62-3.81 (m, 3H), 3.44 (s, 3H), 3.08 (s, 3H), 1.91-2.01 (m, 6H), 1.72-1.79 (m, 1H), 1.48-1.57 (m, 2H), 1.32-1.35 (m, 1H), 1.27 (d, 6H)
442	(400 MHz, $CDCl_3$) δ ppm 13.60 (br s, 1H-NH), 13.23 (br s, 1H-NH), 10.06 (br s, 1H-NH), 7.73-7.84 (d, 5H), 5.04 (septet, 1H), 4.77-4.82 (m, 1H), 4.45 (br s, 2H), 4.07 (br d, 4H), 3.61-3.64 (m, 4H), 3.14 (s, 6H), 2.97 (br s, 3H), 1.91-2.03 (m, 6H), 1.76-1.79 (m, 1H), 1.49-1.62 (m, 2H), 1.33-1.36 (m, 1H), 1.29 (d, 6H)

Cpd Number	^{1}H NMR data
443	(400 MHz, $CDCl_3$) δ ppm 12.34 (br s, 1H-NH), 10.05 (s, 1H-NH), 7.86 (s, 1H), 7.73-7.77 (m, 4H), 5.03 (septet, 1H), 4.76-4.81 (m, 1H), 4.22 (d, 2H), 3.46 (d, 2H), 3.07 (s, 6H), 2.63-2.66 (m, 2H), 2.29-2.33 (m, 2H), 1.76-2.01 (m, 10H), 1.56-1.59 (m, 2H), 1.33-1.35 (m, 2H), 1.28 (d, 6H)
444	(400 MHz, $CDCl_3$) δ ppm 12.92 (br s, 1H-NH), 10.06 (s, 1H-NH), 7.87 (s, 1H), 7.77 (s, 4H), 5.04 (septet, 1H), 4.77-4.83 (m, 1H), 4.28 (s, 2H), 3.08 (s, 6H), 2.80-2.91 (m, 2H), 2.26-2.30 (m, 2H), 1.94-2.10 (m, 10H), 1.78-1.86 (m, 2H), 1.54-1.64 (m, 2H), 1.31 (s, 6H)
445	(400 MHz, $CDCl_3$) δ ppm 12.9 (br s, 1H), 9.99 (br s, 0.5H), 9.79 (br s, 0.5H), 8.00-7.95 (m, 2H), 7.44 (s, 1H), 7.28-7.22 (m, 2H), 4.59-4.49 (m, 2H), 4.06-3.97 (m, 2H), 3.96-3.88 (m, 1H), 3.79-3.72 (m, 1H), 3.70-3.40 (m, 6H), 3.23-2.96 (m, 4H), 2.66-2.37 (m, 5H), 2.21-1.71 (m, 10H), 1.53-1.48 (m,3H)
446	(400 MHz, $CDCl_3$) δ ppm 12.91 (br s, 1H), 9.84 (br s, 0.5H), 9.55 (br s, 0.5H), 8.02-7.95 (m, 2H), 7.44 (s, 1H), 7.30-7.21 (m, 2H), 4.59-4.49 (m, 2H), 4.07-3.97 (m, 2H), 3.96-3.88 (m, 1H), 3.79-3.72 (m, 1H), 3.69-3.55 (m, 3H), 3.53-3.48 (m, 3H), 3.21-2.95 (m, 4H), 2.64-2.40 (m, 5H), 2.22-2.03 (m, 3H), 1.98-1.78 (m, 3H), 1.52-1.48 (m,3H), 1.47-1.43 (m,3H)
447	(400 MHz, $CDCl_3$) δ ppm 13.00 (br s, 1H-NH), 9.94 (br s, 1H-NH), 7.96-8.02 (m, 2H), 7.41 (s, 1H), 7.20-7.26 (m, 2H), 4.47 (t, 2H), 3.98 (d, 2H), 3.91 (t, 1H), 3.86 (t, 2H), 3.75 (t, 2H), 3.67 (d, 2H), 3.55 (d, 2H), 3.23 (s, 3H), 2.90-3.05 (m, 6H), 2.51-2.62 (m, 2H), 2.37-2.46 (m, 2H), 2.22-2.34 (m, 3H), 1.93-2.14 (m, 2H), 1.66-1.78 (m, 2H)

Cpd Number	^{1}H NMR data
448	(300 MHz, $CDCl_3$) δ ppm 7.85 - 7.98 (m, 2 H), 7.38 (s, 1 H), 7.12 - 7.25 (m, 2 H), 4.29 (d, *J*=7.7 Hz, 2 H), 3.93 - 4.10 (m, 4 H), 3.86 (t, *J*=8.3 Hz, 1 H), 3.76 (d, *J*=12.1 Hz, 2 H), 3.60 - 3.71 (m, 2 H), 3.46 (br. s., 2 H), 3.26 (br. s., 1 H), 2.97 (t, *J*=11.9 Hz, 4 H), 2.45 - 2.59 (m, 2 H), 2.30 - 2.42 (m, 4 H), 2.01 - 2.24 (m, 5 H)
AC07	(300 MHz, $CDCl_3$) δ ppm 7.96 (d, *J*=7.7 Hz, 2 H), 7.44 - 7.56 (m, 2 H), 7.37 (s, 1 H), 7.27 - 7.32 (m, 1 H), 4.92 (s, 2 H), 3.91 (quin, *J*=8.4 Hz, 1 H), 3.62 (d, *J*=12.5 Hz, 2 H), 3.22 - 3.40 (m, 5 H), 2.78 - 2.98 (m, 2 H), 2.46 - 2.66 (m, 2 H), 2.24 - 2.44 (m, 2 H), 1.94 - 2.15 (m, 2 H), 1.73 - 1.93 (m, 3 H), 1.35 - 1.67 (m, 3 H)
450	(400 MHz, $CDCl_3$) δ ppm 9.93 (s, 1 H), 7.95 – 7.99 (m, 2 H), 7.46 (s, 1 H), 7.24 – 7.28 (m, 2 H), 3.88 – 3.95 (m, 1 H), 3.81 – 3.85 (m, 2 H), 3.57 – 3.60 (m, 2 H), 3.41 (s, 3 H), 2.25 – 3.31 (m, 1 H), 3.00 – 3.06 (m, 2 H), 2.78 – 2.86 (m, 2 H), 2.44 – 2.65 (m, 8 H), 2.07 – 2.21 (m, 4 H), 1.93 – 2.02 (m, 3 H), 1.39 – 1.49 (m, 1 H
451	(400 MHz, $CDCl_3$) δ ppm 7.86 - 8.07 (m, 2 H), 7.46 (s, 1 H), 7.15 - 7.35 (m, 2 H), 4.42 - 4.57 (m, 1 H), 4.34 (dd, *J*=10.3, 5.0 Hz, 1 H), 4.12 (dd, *J*=10.3, 8.0 Hz, 1 H), 4.03 (t, *J*=7.5 Hz, 1 H), 3.78 - 3.94 (m, 4 H), 3.51 - 3.72 (m, 2 H), 3.31 (br. s., 1 H), 2.96 - 3.17 (m, 3 H), 2.75 - 2.93 (m, 2 H), 2.42 - 2.68 (m, 9 H), 2.31 - 2.40 (m, 1 H), 2.06 - 2.23 (m, 4 H), 1.96 (d, *J*=14.1 Hz, 3 H)

Cpd Number	^{1}H NMR data
453	(400 MHz, pyridine-d_5) δ ppm 8.40 – 8.32 (m, 2H), 7.61 (s, 1H), 7.36 (dd, *J* = 8.5, 7.3 Hz, 2H), 4.27 (d, *J* = 12.9 Hz, 2H), 4.03 (t, *J* = 8.3 Hz, 1H), 3.75 (t, *J* = 4.5 Hz, 4H), 3.57 (d, *J* = 12.4 Hz, 2H), 3.17 (t, *J* = 12.1 Hz, 2H), 3.06 (s, 1H), 2.80 (d, *J* = 12.3 Hz, 4H), 2.66 (td, *J* = 8.9, 2.6 Hz, 2H), 2.55 (s, 4H), 2.42 (d, *J* = 5.8 Hz, 2H), 2.31 (d, *J* = 10.9 Hz, 1H), 2.08 – 1.86 (m, 4H), 1.77 (t, *J* = 12.2 Hz, 4H), 1.64 (s, 3H), 1.25 (s, 2H)
454	(400 MHz, CD_2Cl_2) δ ppm 8.12-8.08 (m, 2H), 7.55 (dd, J = 8.5, 7.4 Hz, 2H), 7.42 (s, 1H), 7.35 (t, J = 7.4 Hz, 1H), 4.00 (p, J = 8.3 Hz, 1H), 3.74-3.66 (m, 2H), 3.63-3.56 (m, 6H), 2.96-2.87 (m, 2H), 2.72-2.53 (m, 7H), 2.48-2.39 (m, 4H), 2.39-2.33 (m, 4H), 2.17-1.97 (m, 6H), 1.92-1.80 (m, 2H), 1.71-1.63 (m, 4H), 1.53-1.46 (m, 2H)
455	(400 MHz, pyridine-d_5) δ ppm 8.42 – 8.30 (m, 2H), 7.57 (s, 1H), 7.41 – 7.32 (m, 2H), 7.17 (d, *J* = 1.2 Hz, 1H), 4.03 (p, *J* = 8.3 Hz, 1H), 3.74 (dt, *J* = 15.6, 4.8 Hz, 8H), 3.54 (d, *J* = 12.4 Hz, 2H), 2.79 (t, *J* = 11.9 Hz, 2H), 2.66 (dq, *J* = 11.4, 8.9 Hz, 2H), 2.57 (t, *J* = 4.6 Hz, 5H), 2.42 (td, *J* = 7.6, 6.6, 3.8 Hz, 2H), 2.37 (t, *J* = 5.0 Hz, 6H), 2.09 (s, 3H), 2.05 – 1.92 (m, 4H), 1.77 (q, *J* = 11.3 Hz, 2H)
456	(400 MHz, pyridine-d_5) δ ppm 8.44 – 8.24 (m, 2H), 7.57 (s, 1H), 7.39 – 7.27 (m, 2H), 7.15 (s, 4H), 4.02 (p, *J* = 8.3 Hz, 1H), 3.75 (t, *J* = 4.6 Hz, 4H), 3.53 (d, *J* = 12.4 Hz, 2H), 3.06 (s, 6H), 2.78 (t, *J* = 11.8 Hz, 2H), 2.66 (dq, *J* = 11.4, 8.9 Hz, 2H), 2.53 (s, 4H), 2.42 (dt, *J* = 10.7, 4.3 Hz, 3H), 2.30 (t, *J* = 10.7 Hz, 1H), 2.06 – 1.89 (m, 4H), 1.73 (q, *J* = 11.6, 11.2 Hz, 2H)

Cpd Number	^{1}H NMR data
457	(400 MHz, pyridine-d_5) δ ppm 8.43 – 8.25 (m, 2H), 7.61 (s, 1H), 7.45 (t, J = 7.8 Hz, 2H), 7.28 – 7.19 (m, 1H), 4.13 – 4.06 (m, 3H), 4.01 – 3.91 (m, 1H), 3.58 (d, J = 12.7 Hz, 2H), 3.02 – 2.79 (m, 8H), 2.74 – 2.59 (m, 3H), 2.53 (d, J = 8.2 Hz, 2H), 2.25 – 2.15 (m, 2H), 2.15 – 1.96 (m, 4H), 1.96 – 1.69 (m, 6H), 1.60 (t, J = 12.4 Hz, 1H), 1.13 (td, J = 7.1, 0.9 Hz, 2H)
458	(400 MHz, pyridine-d_5) δ ppm 8.39 – 8.33 (m, 2H), 7.61 (s, 1H), 7.49 (dd, J = 8.6, 7.4 Hz, 2H), 7.26 (t, J = 7.4 Hz, 1H), 4.11 (d, J = 8.2 Hz, 1H), 3.60 (d, 2H), 3.38 (dd, J = 9.5, 5.0 Hz, 2H), 3.26 (s, 5H), 3.09 (d, J = 5.4 Hz, 2H), 2.86 (s, 7H), 2.76 – 2.64 (m, 5H), 2.5 (m, 2H), 2.58 – 2.46 (m, 4H), 2.08 (d, J = 6.0 Hz, 5H), 1.93 – 1.74 (m, 9H), 1.73 – 1.62 (m, 4H), 1.58 (s, 2H)
459	(400 MHz, pyridine-d_5) δ ppm 8.40 – 8.34 (m, 2H), 7.59 (s, 1H), 7.48 – 7.41 (m, 2H), 7.26 (d, J = 7.6 Hz, 1H), 4.82 – 4.64 (m, 1H), 3.81 – 3.64 (m, 4H), 3.60 (s, 1H), 3.02 – 2.84 (m, 2H), 2.75 (d, J = 22.5 Hz, 4H), 2.71 – 2.63 (m, 2H), 2.63 – 2.56 (m, 1H), 2.51 (q, J = 8.2 Hz, 2H), 2.12 – 1.96 (m, 4H), 1.96 – 1.82 (m, 4H), 1.79 (s, 1H), 1.65 – 1.43 (m, 2H)
460	(400 MHz, pyridine-d_5) δ ppm 8.41 – 8.32 (m, 2H), 7.58 (s, 1H), 7.49 – 7.41 (m, 2H), 7.26 (d, J = 7.3 Hz, 1H), 4.14 – 4.04 (m, 2H), 3.69 (s, 2H), 3.61 (d, J = 12.5 Hz, 2H), 2.91 (d, J = 10.0 Hz, 5H), 2.73 – 2.61 (m, 2H), 2.58 – 2.47 (m, 3H), 2.42 (d, J = 3.1 Hz, 2H), 2.16 (s, 4H), 2.11 – 2.01 (m, 3H), 1.86 (d, J = 3.3 Hz, 3H), 1.82 (d, J = 17.2 Hz, 4H), 1.66 – 1.53 (m, 2H)

Cpd Number	^{1}H NMR data
461	(400 MHz, pyridine-d_5) δ ppm 8.40 – 8.33 (m, 2H), 7.58 (s, 1H), 7.47 (t, J = 7.8 Hz, 2H), 7.28 – 7.18 (m, 1H), 4.10 (t, J = 8.1 Hz, 1H), 3.61 (d, J = 12.5 Hz, 2H), 2.92 (t, J = 12.0 Hz, 2H), 2.83 (s, 3H), 2.75 – 2.64 (m, 4H), 2.52 (t, J = 8.7 Hz, 2H), 2.16 – 2.00 (m, 4H), 1.98 – 1.88 (m, 3H), 1.86 – 1.78 (m, 4H), 1.68 (s, 3H), 1.64 – 1.51 (m, 2H), 0.99 – 0.88 (m, 2H)
462	(400 MHz, pyridine-d_5) δ ppm 8.45 (s, 2H), 8.41 – 8.32 (m, 2H), 7.61 (s, 1H), 7.43 (t, J = 7.7 Hz, 2H), 7.17 (t, J = 1.3 Hz, 24H), 4.10 (p, J = 7.9 Hz, 2H), 3.60 (d, J = 12.6 Hz, 2H), 3.37 (tt, J = 8.5, 4.8 Hz, 1H), 2.91 (t, J = 12.0 Hz, 2H), 2.83 (s, 3H), 2.75 – 2.64 (m, 4H), 2.52 (s, 2H), 2.14 – 2.00 (m, 4H), 1.94 – 1.78 (m, 6H), 1.61 (dd, J = 18.2, 7.1 Hz, 2H), 1.56 – 1.47 (m, 2H), 1.09 – 1.00 (m, 2H)
463	(400 MHz, pyridine-d_5) δ ppm 8.39 – 8.31 (m, 2H), 7.58 (s, 1H), 7.43 (dd, J = 8.7, 7.3 Hz, 2H), 7.22 (t, J = 7.3 Hz, 1H), 4.11 (q, J = 8.2 Hz, 2H), 3.77 (q, J = 7.3 Hz, 2H), 3.60 (d, J = 12.5 Hz, 2H), 2.94 – 2.86 (m, 2H), 2.83 (s, 4H), 2.75 – 2.65 (m, 4H), 2.52 (s, 2H), 2.09 (ddd, J = 19.7, 14.0, 9.5 Hz, 4H), 1.89 (dd, J = 9.2, 5.2 Hz, 1H), 1.86 – 1.78 (m, 5H), 1.59 (d, J = 10.5 Hz, 2H), 1.42 (t, J = 7.4 Hz, 3H)
464	(400 MHz, pyridine-d_5) δ ppm 8.38 – 8.30 (m, 2H), 7.55 (s, 1H), 7.41 (t, J = 7.8 Hz, 2H), 7.19 (t, J = 7.5 Hz, 1H), 4.08 (t, J = 5.9 Hz, 2H), 3.95 (t, J = 6.0 Hz, 2H), 3.56 (d, J = 12.5 Hz, 2H), 3.18 (s, 3H), 2.94 – 2.82 (m, 4H), 2.76 – 2.60 (m, 4H), 2.49 (dd, J = 10.9, 5.8 Hz, 2H), 2.07 (ddd, J = 18.7, 12.5, 8.8 Hz, 4H), 1.97 – 1.72 (m, 4H), 1.67 – 1.49 (m, 2H)

Cpd Number	^{1}H NMR data
465	(400 MHz, pyridine-d_5) δ ppm 8.41 – 8.25 (m, 2H), 7.49 (d, J = 1.9 Hz, 1H), 7.27 (t, J = 7.4 Hz, 2H), 3.61 (d, J = 12.5 Hz, 2H), 2.97 – 2.86 (m, 2H), 2.75 – 2.65 (m, 6H), 2.58 – 2.43 (m, 4H), 2.16 – 1.94 (m, 4H), 1.89 – 1.71 (m, 6H), 1.63 (s, 10H), 1.58 – 1.47 (m, 2H)
466	(400 MHz, $CDCl_3$) δ ppm 13.18 (br s, 1H-NH), 9.81 (br s, 1H-NH), 7.91-7.96 (m, 2H), 7.59 (s, 1H), 7.15-7.25 (m, 2H), 4.40 (t, 2H), 4.03 (d, 2H), 3.88-3.92 (m, 1H), 3.72-3.79 (m, 2H), 3.48-3.57 (m, 4H), 3.26-3.41 (m, 1H), 2.97-3.08 (m, 4H), 2.36-2.61 (m, 5H), 2.00-2.28 (m, 5H), 1.41 (t, 3H)
467	(400 MHz, $CDCl_3$) δ ppm 13.47 (br s, 1H-NH), 10.10 (s, 1H-NH), 7.88 (s, 1H), 7.81 (dd, 4H), 5.06 (pentet, 1H), 4.75-4.81 (m, 1H), 4.52-4.59 (m, 1H), 4.26-4.38 (m, 5H), 4.12 (dd, 1H), 4.02-4.08 (m, 1H), 3.96 (dd, 1H), 3.86-3.91 (m, 1H), 3.37 (d, 1H), 2.88-2.96 (m, 2H), 2.56-2.64 (m, 1H), 2.34-2.47 (m, 3H), 1.93-2.07 (m, 8H), 1.76-1.84 (m, 2H), 1.54-1.71 (m, 4H), 1.25-1.38 (m, 2H)
468	(400 MHz, $CDCl_3$) δ ppm 14.87 (br s, 1H-NH), 12.10 (br s, 1H-NH), 8.22 (br s, 2H), 7.45 (s, 1H), 7.12 (br s, 2H), 5.00-5.02 (m, 1H), 4.30-4.45 (m, 2H), 3.75-4.14 (m, 10H), 3.49-3.71 (m, 1H), 3.11-3.29 (m, 1H), 2.80 (d, 1H), 2.24-2.54 (m, 5H), 175-2.11 (m, 8H), 1.46-1.60 (m, 2H), 1.23-1.37 (m, 2H)
469	(400 MHz, $CDCl_3$) δ ppm 14.96 (br s, 1H-NH), 11.11 (br s, 1H-NH), 8.23 (br s, 2H), 7.45 (s, 1H), 7.10 (br s, 2H), 5.01-5.19 (m, 1H), 4.74-4.78 (m, 1H), 3.70-4.16 (m, 5H), 3.49-3.64 (m, 1H), 3.10-3.29 (m, 1H), 3.04 (s, 6H), 2.77-2.88 (m, 2H), 2.37-2.64 (m, 4H), 1.91-2.12 (m, 5H), 1.24-1.79 (m, 6H)

Cpd Number	^{1}H NMR data
471	(400 MHz, $CDCl_3$) δ ppm 13.30 (br s, 1H-NH), 9.98 (s, 1H), 7.96-8.01 (m, 2H), 7.42 (s, 1H), 721-7.26 (m, 2H), 4.63-4.66 (m, 1H), 4.43 (t, 2H), 4.03 (d, 2H), 3.87-3.94 (m, 1H), 3.78 (d, 2H), 3.60 (br s, 4H), 3.46-3.53 (m, 2H), 3.25 (s, 3H), 3.08 (s, 3H), 2.88-2.99 (m, 4H), 2.54-2.63 (m, 2H), 2.41-2.47 (m, 4H), 2.27-2.32 (m, 2H), 2.02-2.17 (m, 2H)
473	(400 MHz, $CDCl_3$) δ ppm 8.93 (br. s., 1 H), 8.71 (br. s., 1 H), 8.62 (br. s., 1 H), 7.66 (s, 1 H), 4.21 (d, *J*=8.6 Hz, 2 H), 3.96 (t, *J*=8.2 Hz, 1 H), 3.82 (br. s., 1 H), 3.62 - 3.76 (m, 4 H), 3.48 (s, 3 H), 3.42 (s, 3 H), 3.39 (d, *J*=6.1 Hz, 2 H), 3.09 (t, *J*=12.0 Hz, 2 H), 2.55 - 2.72 (m, 2 H), 2.49 (d, *J*=7.6 Hz, 2 H), 2.29 (d, *J*=12.0 Hz, 2 H), 2.10 - 2.21 (m, 3 H), 1.88 - 2.07 (m, 6 H)
474	(300 MHz, $CDCl_3$) δ ppm 7.83 - 8.03 (m, 2 H), 7.34 (s, 1 H), 7.08 - 7.24 (m, 2 H), 3.94 - 4.25 (m, 8 H), 3.85 (dt, *J*=16.8, 8.3 Hz, 2 H), 3.62 - 3.72 (m, 2 H), 3.57 (d, *J*=12.5 Hz, 2 H), 2.97 - 3.11 (m, 2 H), 2.86 (t, *J*=11.4 Hz, 2 H), 2.42 - 2.61 (m, 2 H), 2.24 - 2.38 (m, 2 H), 1.72 - 2.11 (m, 7 H), 1.42 - 1.64 (m, 3 H), 1.36 (s, 1 H)
476	(400 MHz, $CDCl_3$) δ ppm 13.60 (br s, 1H), 10.09 (br s, 1H), 7.81 (s, 1H), 7.41 (s, 4H), 4.93-4.85 (m, 1H), 4.40-4.32 (m, 2H), 4.06-4.00 (m, 2H), 3.57-3.51 (m, 2H), 3.48-3.39 (m, 3H), 3.32-3.25 (m, 2H), 3.08 (s, 6H), 3.00-2.89 (m, 2H), 2.30-2.08 (m, 4H), 2.04-1.95 (m, 4H), 1.90-1.75 (m, 5H), 1.68-1.60 (m, 2H), 1.45-1.35 (m, 1H)

Cpd Number	^{1}H NMR data
481	(400 MHz, $CDCl_3$) δ ppm 13.32 (br s, 1H-NH), 10.06 (s, 1H-NH), 7.88 (s, 1H), 7.78-7.83 (m, 4H), 5.06 (pentet, 1H), 4.75-4.81 (m, 1H), 4.27-4.35 (m, 4H), 3.94-3.97 (m, 2H), 3.37-3.40 (m, 2H), 3.08 (s, 6H), 2.90-2.94 (m, 2H), 2.41-2.44 (m, 2H), 1.92-2.04 (m, 5H), 1.78-1.83 (m, 4H), 1.56-1.654 (m, 3H), 1.24-1.37 (m, 2H)
482	(400 MHz, $CDCl_3$) δ ppm 13.37 (s, 1H-NH), 9.92 (s, 1H-NH), 7.97-8.00 (m, 2H), 7.43 (s, 1H), 7.23-7.27 (m, 2H), 4.41-4.47 (m, 2H), 4.29 (pentet, 1H), 4.04-4.07 (m, 2H), 3.91 (t, 1H), 3.80-3.82 (m, 2H), 3.50-3.53 (m, 2H), 3.23-3.31 (m, 1H), 3.00-3.04 (m, 4H), 2.97 (s, 3H), 2.56-2.63 (m, 2H), 2.43-2.47 (m, 3H), 2.26-2.29 (m, 2H), 2.07-2.12 (m, 3H), 1.17 (d, 6H)
483	(400 MHz, $CDCl_3$) δ ppm 13.32 (s, 1H-NH), 9.90 (s, 1H-NH), 7.95-8.00 (m, 2H), 7.42 (s, 1H), 7.21-7.26 (m, 2H), 4.39-4.45 (m, 2H), 4.04-4.07 (m, 2H), 3.74-3.95 (m, 3H), 3.51-3.55 (m, 2H), 3.42 (q, 2H), 3.24-3.31 (m, 1H), 3.02 (s, 3H), 2.52-2.63 (m, 2H), 2.35-2.45 (m, 4H), 2.26-2.29 (m, 2H), 2.01-2.17 (m, 3H), 1.68-1.89 (m, 3H), 1.20 (t, 3H)
484	(400 MHz, $CDCl_3$) δ ppm 13.23 (s, 1H-NH), 9.93 (s, 1H-NH), 7.93-7.99 (m, 2H), 7.44 (s, 1H), 7.20-7.25 (m, 2H), 4.39-4.45 (m, 2H), 4.29-4.32 (m, 2H), 4.13-4.21 (m, 2H), 4.03-4.06 (m, 2H), 3.87-3.93 (m, 1H), 3.76-3.82 (m, 2H), 3.51-3.54 (m, 2H), 3.27-3.24 (m, 2H), 3.24 (s, 3H), 2.98-3.08 (m, 4H), 2.53-2.63 (m, 2H), 2.43-2.47 (m, 4H), 2.27-2.29 (m, 2H), 2.01-2.17 (m, 2H)

Cpd Number	^{1}H NMR data
485	(400 MHz, $CDCl_3$) δ ppm 13.32 (br s, 1H-NH), 9.90 (s, 1H-NH), 7.95-8.00 (m, 2H), 7.42 (s, 1H), 7.17-7.26 (m, 2H), 4.40-4.46 (m, 2H), 4.04-4.07 (m, 2H), 3.89 (pentet, 1H), 3.74-3.79 (m, 2H), 3.50-3.59 (m, 6H), 3.23-3.31 (m, 1H), 2.96-3.06 (m, 4H), 2.52-2.63 (m, 2H), 2.41-2.49 (m, 4H), 2.24-2.32 (m, 2H), 2.02-2.17 (m, 2H), 1.06-1.957 (m, 4H)
487	(400 MHz, $CDCl_3$) δ ppm 13.52 (s, 1H-NH), 9.89 (s, 1H-NH), 7.96-7.99 (m, 2H), 7.43 (s, 1H), 7.23-7.29 (m, 2H), 4.39-4.45 (m, 2H), 3.98-4.07 (m, 2H), 3.75-3.93 (m, 9H), 3.46-3.04 (m, 5H), 3.23-3.34 (m, 1H), 3.04 (br s, 3H), 2.53-2.61 (m, 2H), 2.36-2.46 (m, 3H), 2.21-2.29 (m, 2H), 2.03-2.16 (m, 2H), 1.73-1.81 (m, 1H)
488	(400 MHz, $CDCl_3$) δ ppm, 12.52 ppm (s, 1H), 9.89 ppm (s, 1H), 8.0 ppm (dd, J=9.1, 4.55 Hz, 2H), 7.44 ppm (s, 1H), 7.28-7.23 ppm (m, 2H), 3.94-3.76 ppm (m, 8H), 3.61-3.55 ppm (m, 2H), 3.32-3.23 ppm (m, 4H), 3.03 ppm (t, J=12.13 Hz, 2H), 2.86-2.77 ppm (m, 2H), 2.65-2.41 ppm (m, 9H), 2.21-2.05 ppm (m, 4H), 1.96 ppm (m, 4H), 1.51-1.4 ppm (m, 2H)
489	(400 MHz, $CDCl_3$) δ ppm 8.29 – 8.31 (m, 1 H), 7.79 (s, 1 H), 7.51 – 7.53 (m, 2 H), 4.17 – 4.18 (m, 2 H), 4.05 – 4.09 (m, 2 H), 3.88 – 3.90 (m, 4 H), 3.60 – 3.63 (m, 4 H), 3.47 – 3.55 (m, 3 H), 3.07 (s, 6 H), 2.21 – 2.27 (m, 1 H), 1.79 – 1.82 (m, 2 H), 1.55 – 1.63 (m, 3 H), 1.45 – 1.47 (m, 6 H)

Cpd Number	^{1}H NMR data
490	(400 MHz, $CDCl_3$) δ ppm 7.95 - 8.06 (m, 2 H), 7.46 (s, 1 H), 7.21 - 7.32 (m, 2 H), 4.10 (d, *J*=11.4 Hz, 2 H), 3.98 (quin, *J*=8.4 Hz, 1 H), 3.75 (d, *J*=12.6 Hz, 2 H), 3.38 - 3.55 (m, 2 H), 3.10 - 3.23 (m, 2 H), 3.03 - 3.10 (m, 6 H), 2.91 - 3.03 (m, 3 H), 2.57 - 2.73 (m, 2 H), 2.49 - 2.55 (m, 3 H), 2.39 - 2.49 (m, 2 H), 1.96 - 2.19 (m, 6 H), 1.76 - 1.89 (m, 4 H)
492	(400 MHz, $CDCl_3$) δ ppm, 13.63 ppm (s, 1H), 9.86 ppm (s, 1H), 7.99 ppm (dd, J=9.1, 4.8 Hz, 2H), 7.45 ppm (s, 1H), 7.28-7.24 ppm (m, 2H), 4.41-4.21 ppm (m, 2H), 4.0-3.7 ppm (m, 10H), 3.55 ppm (d, J=11.37 Hz, 2H), 3.35-3.25 ppm (m, 1H), 2.95 ppm (m, 10H), 2.61 ppm (m, 2H), 2.46 ppm (m, 4H), 2.27-2.06 ppm (m, 4H)
494	(400 MHz, $CDCl_3$) δ ppm 13.28 (br s, 1H-NH), 9.83 (br s, 1H-NH), 7.96-8.00 (m, 2H), 7.44 (s, 1H), 7.23-7.28 (m, 2H), 4.49 (t, 2H), 4.00 (dd, 2H), 3.93 (t, 1H), 3.71 (d, 2H), 3.59 (q, 2H), 3.53 (d, 2H), 2.88-3.05 (m, 6H), 2.53-2.64 (m, 2H), 2.39-2.47
496	(400 MHz, $CDCl_3$) δ ppm 9.91 (s, 1 H), 7.94 – 7.97 (m, 3 H), 7.24 – 7.27 (m, 2 H), 4.43 (br. s, 2 H), 4.17 – 4.23 (q, 2 H), 3.46 – 3.54 (m, 2 H), 3.43 (s, 3 H), 2.90 – 2.98 (m, 2 H), 1.82 – 1.95 (m, 3 H), 1.58 (br. s, 1 H), 1.51 – 1.55 (d, 6 H), 1.29 – 1.33 (t, 3 H)
497	(400 MHz, $CDCl_3$) δ ppm 9.79 (s, 1 H), 7.83 - 7.95 (m, 3 H), 7.09 - 7.26 (m, 2 H), 4.35 (br. s., 2 H), 4.13 (q, *J*=7.2 Hz, 2 H), 3.29 - 3.50 (m, 2 H), 2.99 (s, 3 H), 2.81 - 3.07 (m, 2 H), 1.73 - 1.93 (m, 4 H), 1.53 (br. s., 2 H), 1.37 - 1.48 (m, 6 H), 1.15 - 1.28 (m, 4 H)

Cpd Number	^{1}H NMR data
499	(HCl salt) (400 MHz, $CDCl_3$) δ ppm 9.84 - 10.10 (m, 1 H), 8.16 (d, *J*=7.3 Hz, 1 H), 7.73 (t, *J*=2.2 Hz, 1 H), 7.68 (dd, *J*=8.1, 1.2 Hz, 1 H), 7.36 - 7.51 (m, 2 H), 6.87 - 7.00 (m, 1 H), 3.88 - 4.01 (m, 5 H), 3.69 - 3.85 (m, 4 H), 3.19 - 3.27 (m, 3 H), 2.92 - 3.06 (m, 9 H), 2.53 - 2.68 (m, 3 H), 2.39 - 2.49 (m, 4 H), 2.02 - 2.22 (m, 3 H), 1.86 (dt, *J*=6.7, 3.2 Hz, 2 H)
500	(300 MHz, $CDCl_3$) δ ppm 13.35 (br. s., 1 H), 9.78 (s, 1 H), 8.20 (d, *J*=8.4 Hz, 2 H), 7.75 (d, *J*=8.4 Hz, 2 H), 7.41 (s, 1 H), 4.22 - 4.52 (m, 2 H), 4.00 (d, *J*=11.4 Hz, 2 H), 3.86 (quin, *J*=8.2 Hz, 1 H), 3.75 (d, *J*=12.5 Hz, 2 H), 3.46 (d, *J*=11.4 Hz, 2 H), 3.22 (br. s., 1 H), 2.83 - 3.03 (m, 9 H), 2.47 - 2.72 (m, 2 H), 2.32 - 2.47 (m, 4 H), 2.16 - 2.30 (m, 2 H), 1.88 - 2.14 (m, 3 H)
501	(300 MHz, $CDCl_3$) δ ppm 7.87 - 8.05 (m, 2 H), 7.46 - 7.65 (m, 3 H), 7.32 - 7.42 (m, 1 H), 3.87 - 4.04 (m, 1 H), 3.56 - 3.69 (m, 3 H), 3.49 (d, *J*=12.9 Hz, 2 H), 3.27 - 3.39 (m, 2 H), 3.24 (s, 3 H), 2.53 - 2.77 (m, 4 H), 2.31 - 2.50 (m, 2 H), 1.86 - 2.18 (m, 5 H), 1.27 (t, *J*=6.9 Hz, 3 H)
503	(300 MHz, $CDCl_3$) δ ppm 7.89 - 8.01 (m, 2 H), 7.48 - 7.58 (m, 3 H), 7.32 - 7.43 (m, 1 H), 4.07 (t, *J*=8.4 Hz, 1 H), 3.66 - 3.73 (m, 4 H), 3.60 – 3.64 (m, 1 H), 3.46 - 3.58 (m, 3 H), 3.37 (s, 3 H), 3.12 - 3.29 (m, 4 H), 2.95 - 3.11 (m, 1 H), 2.52 - 2.61 (m, 2 H), 2.38 - 2.52 (m, 2 H), 2.22 (d, *J*=12.0 Hz, 1 H), 1.93 - 2.15 (m, 3 H), 1.68 - 1.91 (m, 2 H)

Cpd Number	^{1}H NMR data
504	(400 MHz, $CDCl_3$) δ ppm 7.97 - 8.06 (m, 2 H), 7.47 (s, 1 H), 7.19 - 7.32 (m, 2 H), 4.09 (t, *J*=7.6 Hz, 1 H), 3.98 (t, *J*=8.4 Hz, 1 H), 3.70 - 3.80 (m, 5 H), 3.29 - 3.50 (m, 4 H), 2.98 - 3.09 (m, 3 H), 2.47 - 2.74 (m, 8 H), 2.43 (dd, *J*=11.4, 4.7 Hz, 4 H), 2.03 - 2.15 (m, 3 H), 1.70 - 2.02 (m, 5 H)
505	(300 MHz, DMSO-d_6) δ ppm 8.04 - 8.24 (m, 2 H), 7.24 (t, *J*=8.8 Hz, 2 H), 7.06 (s, 1 H), 3.77 (dd, *J*=16.3, 8.1 Hz, 4 H), 3.54 (d, *J*=12.3 Hz, 2 H), 3.27 - 3.40 (m, 3 H), 3.03 - 3.22 (m, 4 H), 2.70 - 2.93 (m, 3 H), 2.21 - 2.41 (m, 8 H), 2.14 (d, *J*=10.9 Hz, 1 H), 1.86 - 2.00 (m, 1 H), 1.79 (d, *J*=9.4 Hz, 4 H), 1.61 (dt, *J*=8.7, 4.5 Hz, 1 H), 1.20 (s, 3 H)
507	(400 MHz, $CDCl_3$) δ ppm 9.94 (s, 1 H), 7.89 - 8.05 (m, 2 H), 7.49 (s, 1 H), 7.18 - 7.34 (m, 2 H), 4.48 (t, *J*=12.2 Hz, 2 H), 4.09 (d, *J*=11.1 Hz, 2 H), 3.94 (t, *J*=8.3 Hz, 1 H), 3.85 (d, *J*=11.8 Hz, 2 H), 3.46 - 3.59 (m, 2 H), 3.29 (br. s., 1 H), 2.95 - 3.15 (m, 5 H), 2.55 - 2.71 (m, 2 H), 2.40 - 2.54 (m, 4 H), 2.32 (d, *J*=10.7 Hz, 2 H), 2.03 - 2.20 (m, 2 H), 1.44 - 1.56 (m, 2 H), 1.11 - 1.21 (m, 2 H)
508	(400 MHz, $CDCl_3$) δ ppm 9.85 (s, 1 H), 7.89 - 8.08 (m, 2 H), 7.48 (s, 1 H), 7.20 - 7.33 (m, 2 H), 4.48 (t, *J*=12.1 Hz, 2 H), 4.08 (d, *J*=11.8 Hz, 2 H), 3.94 (t, *J*=8.3 Hz, 1 H), 3.85 (d, *J*=12.5 Hz, 2 H), 3.53 (d, *J*=11.3 Hz, 2 H), 3.27 (br. s., 1 H), 2.89 - 3.16 (m, 4 H), 2.55 - 2.69 (m, 2 H), 2.42 - 2.52 (m, 4 H), 2.25 - 2.37 (m, 2 H), 2.03 - 2.22 (m, 2 H), 1.79 - 1.88 (m, 3 H), 1.60 (s, 4 H)

Cpd Number	^{1}H NMR data
509	(HCl salt) (400 MHz, $CDCl_3$) δ ppm 13.52 (br. s., 1 H), 10.03 (br. s., 1 H), 7.69 - 7.86 (m, 2 H), 7.35 - 7.53 (m, 2 H), 7.21 (d, *J*=7.6 Hz, 1 H), 4.47 (t, *J*=12.1 Hz, 2 H), 4.08 (d, *J*=11.5 Hz, 2 H), 3.89 - 4.02 (m, 1 H), 3.84 (d, *J*=12.7 Hz, 2 H), 3.52 (d, *J*=11.0 Hz, 2 H), 3.41 (s, 3 H), 3.21 - 3.33 (m, 1 H), 2.89 - 3.15 (m, 3 H), 2.54 - 2.75 (m, 2 H), 2.40 - 2.54 (m, 6 H), 2.21 - 2.37 (m, 2 H), 1.96 - 2.21 (m, 3 H)
510	(400 MHz, $CDCl_3$) δ ppm 8.27 (d, *J*=8.6 Hz, 2 H), 7.82 (d, *J*=8.8 Hz, 2 H), 7.49 (s, 1 H), 4.34 (d, *J*=9.0 Hz, 2 H), 4.02 - 4.14 (m, 2 H), 3.88 - 3.98 (m, 1 H), 3.76 - 3.86 (m, 2 H), 3.49 - 3.60 (m, 2 H), 3.42 (s, 3 H), 2.95 - 3.12 (m, 3 H), 2.54 - 2.65 (m, 2 H), 2.40 - 2.51 (m, 4 H), 2.17 - 2.36 (m, 3 H), 2.03 - 2.17 (m, 4 H)
511	(HCl salt) (400 MHz, $CDCl_3$) δ ppm 13.45 (br.s, 1 H), 7.83 – 7.86 (m, 1 H), 7.78 – 7.81 (m, 1 H), 7.44 (s, 1 H), 7.18 – 7.22 (t, 1 H), 4.43 – 4.49 (m, 2 H), 4.06 – 4.10 (m, 2 H), 3.90 – 3.96 (m, 1 H), 3.82 – 3.85 (m, 3 H), 3.53 (br. s, 2 H), 3.29 (br. s, 1 H), 9.99 – 3.12 (m , 11 H), 2.59 – 2.64 (m, 2 H), 2.42 – 2.48 (m, 4 H), 2.28 – 2.32 (m, 3 H), 2.06 – 2.19 (m, 3 H)
512	(HCl salt) (400 MHz, $CDCl_3$) δ ppm 13.56 (br. s., 1 H), 9.89 (s, 1 H), 7.98 (dd, *J*=8.3, 1.2 Hz, 1 H), 7.86 (dt, *J*=10.3, 2.2 Hz, 1 H), 7.51 - 7.59 (m, 1 H), 7.48 (s, 1 H), 6.96 - 7.13 (m, 1 H), 4.46 (br. s., 2 H), 4.08 (br. s., 2 H), 3.94 (quin, *J*=8.3 Hz, 1 H), 3.74 - 3.86 (m, 2 H), 3.52 (br. s., 2 H), 3.16 - 3.34 (m, 1 H), 2.94 - 3.15 (m, 10 H), 2.56 - 2.76 (m, 2 H), 2.40 - 2.54 (m, 4 H), 2.29 (br. s., 2 H), 2.04 - 2.23 (m, 2 H)

Cpd Number	^{1}H NMR data
513	(HCl salt) (400 MHz, $CDCl_3$) δ ppm 13.42 (br. s., 1 H), 9.87 (s, 1 H), 8.50 (s, 1 H), 8.33 (d, *J*=8.3 Hz, 1 H), 7.65 - 7.77 (m, 1 H), 7.52 - 7.64 (m, 1 H), 7.47 (s, 1 H), 4.46 (t, *J*=11.5 Hz, 2 H), 4.08 (d, *J*=11.7 Hz, 2 H), 3.94 (t, *J*=8.3 Hz, 1 H), 3.83 (d, *J*=12.0 Hz, 2 H), 3.53 (d, *J*=9.5 Hz, 2 H), 3.30 (br.s, 1H), 3.06 (br. s., 8 H), 3.00- 3.03 (m, 2 H), 2.56 - 2.73 (m, 2 H), 2.38 - 2.54 (m, 4 H), 2.24 - 2.38 (m, 2 H), 2.00 - 2.24 (m, 2 H)
514	(300 MHz, $CDCl_3$) δ ppm 7.62 - 7.81 (m, 2 H), 7.37 (s, 1 H), 7.12 (t, *J*=9.0 Hz, 1 H), 3.76 - 4.02 (m, 4 H), 3.69 (d, *J*=12.8 Hz, 2 H), 3.34 (s, 3 H), 2.83 - 3.00 (m, 3 H), 2.78 (br. s., 2 H), 2.45 - 2.64 (m, 3 H), 2.27 - 2.45 (m, 6 H), 2.20 (s, 3 H), 1.76 - 2.12 (m, 5 H)
515	(300 MHz, $CDCl_3$) δ ppm 13.44 (br. s., 1 H), 9.87 (br. s., 1 H), 7.86 (d, *J*=8.4 Hz, 1 H), 7.68 - 7.80 (m, 1 H), 7.33 - 7.53 (m, 2 H), 6.93 - 7.08 (m, 1 H), 4.21 - 4.53 (m, 2 H), 4.00 (d, *J*=12.8 Hz, 2 H), 3.63 - 3.90 (m, 3 H), 3.45 (d, *J*=11.7 Hz, 2 H), 3.36 (s, 3 H), 3.20 (br.s, 1 H), 2.81 - 3.10 (m, 4 H), 2.48 - 2.63 (m, 2 H), 2.40 (br. s., 4 H), 2.15 - 2.27 (m, 2 H), 1.96 - 2.13 (m, 2 H)
516	(HCl salt) (300 MHz, $CDCl_3$) δ ppm 8.36 (s, 1 H), 8.24 (d, *J*=8.1 Hz, 1 H), 7.48 - 7.70 (m, 2 H), 7.41 (s, 1 H), 4.38 (br. s., 2 H), 4.02 (br. s., 2 H), 3.83 - 3.92 (m, 1 H), 3.76 (d, *J*=12.8 Hz, 1 H), 3.58 - 3.71 (m, 1 H), 3.43 (br. s., 2 H), 3.35 (s, 3 H), 3.13 - 3.24 (m, 1 H), 2.84 - 3.07 (m, 4 H), 2.50 - 2.66 (m, 2 H), 2.41 (br. s., 4 H), 2.16 - 2.30 (m, 2 H), 2.07 (dd, *J*=16.3, 8.6 Hz, 2 H)

Cpd Number	^{1}H NMR data
522	(400 MHz, $CDCl_3$) δ ppm 13.21 (1H, s), 9.86 (1H, s), 7.99 (2H, m), 7.45 (1H, s), 7.19 (2H, m), 3.84 (1H, m), 3.76 (2H, d), 3.63 (3H, s), 3.56 (1H, d), 3.20 (5H, m), 2.95 (7H, m), 2.45 (6H, m), 2.08 (6H, m)
523	(400 MHz, $CDCl_3$) δ ppm 9.92 (br. s., 1 H), 7.92 - 8.07 (m, 2 H), 7.47 (s, 1 H), 7.10 - 7.32 (m, 1 H), 3.97 (t, *J*=8.4 Hz, 1 H), 3.64 - 3.72 (m, 2 H), 3.50 - 3.63 (m, 2 H), 3.36 - 3.44 (m, 2 H), 3.32 (q, *J*=7.3 Hz, 1 H), 3.03 - 3.09 (m, 6 H), 2.91 - 3.03 (m, 2 H), 2.49 - 2.68 (m, 2 H), 2.30 - 2.47 (m, 3 H), 1.99 - 2.17 (m, 2 H), 1.92 (d, *J*=10.6 Hz, 2 H), 1.53 - 1.69 (m, 3 H)
524	(400 MHz, $CDCl_3$) δ ppm 8.00 – 8.04 (m, 2 H), 7.46 (s, 1 H), 7.24 – 7.29 (m, 2 H), 3.96 – 4.05 (m, 2 H), 3.68 – 3.78 (m, 2 H), 3.34 (s, 3 H), 3.20 (br. s, 1 H), 3.06 (s, 6 H), 2.88 - 2.98 (5 H), 2.56 – 2.65 (m, 3 H), 2.39 – 2.46 (m, 2 H), 2.11 – 2.19 (m, 4 H), 1.98 – 2.07 (m, 4 H)
525	(400 MHz, $CDCl_3$) δ ppm 7.90 - 8.04 (m, 2 H), 7.48 (s, 1 H), 7.16 - 7.32 (m, 2 H), 4.00 (quin, *J*=8.4 Hz, 2 H), 3.72 (d, *J*=12.5 Hz, 2 H), 2.90 - 3.04 (m, 2 H), 2.71 - 2.87 (m, 8 H), 2.57 - 2.67 (m, 4 H), 2.33 - 2.55 (m, 3 H), 2.03 - 2.15 (m, 4 H), 1.91 - 2.01 (m, 4 H), 1.84 (qd, *J*=12.1, 3.6 Hz, 2 H), 1.12 - 1.23 (m, 5 H)
526	(400 MHz, DMSO-d_6) δ ppm 8.25 - 8.41 (m, 2 H), 7.37 - 7.52 (m, 2 H), 7.26 (s, 1 H), 3.98 (t, *J*=8.2 Hz, 1 H), 3.57 (br. s., 1 H), 3.38 (q, *J*=7.0 Hz, 4 H), 3.23 (br. s., 2 H), 2.99 (t, *J*=12.1 Hz, 2 H), 2.92 (s, 6 H), 2.48 - 2.52 (m, 2 H), 2.28 - 2.46 (m, 6 H), 1.92 - 2.18 (m, 4 H), 1.09 (t, *J*=7.0 Hz, 2 H)

Cpd Number	^{1}H NMR data
527	(400 MHz, $CDCl_3$) δ ppm 9.92 (br. s., 1 H), 7.87 - 8.11 (m, 2 H), 7.38 - 7.54 (m, 1 H), 7.16 - 7.32 (m, 2 H), 4.69 (t, *J*=3.6 Hz, 1 H), 4.04 - 4.13 (m, 1 H), 3.92 - 4.02 (m, 1 H), 3.85 (dt, *J*=11.6, 3.4 Hz, 1 H), 3.73 (d, *J*=12.5 Hz, 2 H), 3.04 - 3.12 (m, 6 H), 2.91 - 3.03 (m, 3 H), 2.75 - 2.88 (m, 2 H), 2.51 - 2.71 (m, 4 H), 2.33 - 2.48 (m, 2 H), 1.97 - 2.19 (m, 4 H), 1.75 - 1.93 (m, 2 H), 1.59 (br. s., 2 H)
530	(400 MHz, $CDCl_3$) δ ppm 8.35 (br. s., 1 H), 7.77 - 8.12 (m, 2 H), 7.50 - 7.65 (m, 1 H), 5.29 - 5.57 (m, 1 H), 4.47 (t, *J*=11.5 Hz, 2 H), 4.09 (d, *J*=11.7 Hz, 2 H), 3.75 - 3.99 (m, 3 H), 3.38 - 3.64 (m, 5 H), 3.30 (br. s., 1 H), 3.07 (br. s., 4 H), 2.07 - 2.71 (m, 7 H), 1.49 - 1.50 (m, 6 H), 1.45 (s, 3H), 1.17 - 1.37 (m, 1 H)
531	(400 MHz, $CDCl_3$) δ ppm 9.70 (br. s., 1 H), 8.99 (br. s., 1 H), 8.47 - 8.78 (m, 2 H), 7.65 (s, 1 H), 4.20 (d, *J*=9.3 Hz, 2 H), 3.91 - 4.02 (m, 1 H), 3.60 - 3.86 (m, 5 H), 3.28 - 3.49 (m, 5 H), 2.92 - 3.17 (m, 8 H), 2.43 - 2.70 (m, 4 H), 2.30 (d, *J*=11.2 Hz, 2 H), 2.09 - 2.23 (m, 2 H), 1.84 - 2.05 (m, 5 H), 1.46 - 1.78 (m, 2 H)
532	(400 MHz, $CDCl_3$) δ ppm 8.31 (br. s., 1 H), 7.94 - 8.07 (m, 2 H), 7.21 - 7.32 (m, 3 H), 4.61 (s, 1 H), 4.33 (s, 1 H), 4.21 (d, *J*=9.4 Hz, 1 H), 3.99 (t, *J*=8.4 Hz, 1 H), 3.79 - 3.88 (m, 1 H), 3.69 - 3.77 (m, 2 H), 3.61 (d, *J*=10.4 Hz, 1 H), 3.02 - 3.10 (m, 7 H), 2.83 - 3.02 (m, 3 H), 2.52 - 2.65 (m, 2 H), 2.40 - 2.52 (m, 2 H), 2.25 - 2.39 (m, 3 H), 2.12 - 2.24 (m, 2 H), 2.08 (d, *J*=9.9 Hz, 3 H)

Cpd Number	^{1}H NMR data
534	(400 MHz, $CDCl_3$) δ ppm 12.63 (1H, s), 10.02 (1H, s), 7.79 (1H, s), 7.67 (2H, d), 7.05 (2H, d), 4.99 (1H, m), 4.73 (1H, m), 3.96 (2H, m), 3.74 (2H, d), 3.47 (3H, m), 3.19 (2H, m), 3.01 (6H, s), 1.88 (8H, m), 1.72 (1H, d), 1.52 (1H, m), 1.45 (6H, d), 1.27 (6H, d)
537	(400 MHz, $CDCl_3$) δ ppm 10.02 (br. s., 1 H), 7.91 - 8.11 (m, 2 H), 7.39 - 7.49 (m, 1 H), 7.17 - 7.31 (m, 2 H), 3.90 - 4.12 (m, 2 H), 3.61 - 3.89 (m, 9 H), 2.97 (t, *J*=11.7 Hz, 2 H), 2.56 - 2.74 (m, 6 H), 2.37 - 2.50 (m, 3 H), 2.23 - 2.35 (m, 1 H), 1.99 - 2.17 (m, 4 H), 1.81 (qd, *J*=11.9, 3.3 Hz, 2 H), 1.61 (br. s., 3 H)
538	(400 MHz, $CDCl_3$) δ ppm 7.93 - 8.08 (m, 2 H), 7.41 - 7.50 (m, 1 H), 7.19 - 7.32 (m, 2 H), 3.93 - 4.07 (m, 2 H), 3.76 - 3.85 (m, 4 H), 3.57 - 3.75 (m, 6 H), 3.30 (s, 3 H), 2.96 (t, *J*=11.6 Hz, 2 H), 2.54 - 2.74 (m, 6 H), 2.36 - 2.51 (m, 3 H), 1.96 - 2.19 (m, 6 H), 1.74 - 1.90 (m, 2 H)
539	(300 MHz, $CDCl_3$) δ ppm 8.25 (d, *J*=2.3 Hz, 1 H), 7.97 - 8.10 (m, 2 H), 7.87 (s, 1 H), 7.46 - 7.64 (m, 3 H), 7.26 - 7.40 (m, 1 H), 6.74 (d, *J*=8.8 Hz, 1 H), 3.90 (ddd, *J*=13.7, 7.1, 3.8 Hz, 2 H), 3.51 - 3.74 (m, 3 H), 2.83 - 2.95 (m, 1 H), 2.74 (s, 2 H), 2.21 - 2.51 (m, 2 H), 1.74 - 2.13 (m, 9 H), 1.49 (s, 4 H)
540	(300 MHz, DMSO-d_6) δ ppm 8.25 - 8.43 (m, 2 H), 7.32 - 7.51 (m, 2 H), 7.26 (s, 1 H), 3.90 - 4.09 (m, 3 H), 3.81 (d, *J*=12.6 Hz, 4 H), 3.72 (br. s., 2 H), 3.55 (br. s., 1 H), 3.45 (br. s., 1 H), 3.22 (s, 3 H), 3.10 - 3.26 (m, 4 H), 2.82 - 3.07 (m, 5 H), 2.34 (d, *J*=10.6 Hz, 2 H), 1.89 - 2.22 (m, 4 H), 1.59 - 1.81 (m, 3 H), 1.41 (s, 3 H), 1.22 (d, *J*=15.3 Hz, 4 H)

Cpd Number	^{1}H NMR data
541	(300 MHz, DMSO-d_6) δ ppm 8.23 - 8.44 (m, 2 H), 7.34 - 7.51 (m, 2 H), 7.28 (s, 1 H), 3.99 (t, *J*=8.4 Hz, 2 H), 3.69 (s, 2 H), 3.73 (s, 1 H), 3.00 (t, *J*=12.3 Hz, 2 H), 2.93 (s, 7 H), 2.49 (br. s., 3 H), 2.27 (br. s., 3 H), 1.80 - 2.16 (m, 4 H), 1.41 (s, 6 H)
542	(400 MHz, DMSO-d_6) δ ppm 11.71 (s, 1H), 10.59 (br s, 1H),8.35 (d, 1H), 7.89-7.86 (m, 1H), 7.62 (s, 1H), 7.15 (d, 1H), 5.22-5.12 (m, 1H), 4.57 (d, 2H), 3.65-3.50 (m, 6H), 3.44-3.36 (m, 2H), 3.17-3.07 (m, 2H), 2.94 (s, 6H), 2.25-2.15 (m, 2H), 2.01-1.73 (m, 10H),1.62-1.52 (m, 2H), 1.32 (d, 6H)
544	(zwitterion) (400 MHz, $CDCl_3$) δ ppm 8.43 (s, 1H-NH), 7.91 (s, 1H), 7.78 (d, 2H), 7.50 (d, 2H), 5.06 (septet, 1H), 4.78-4.81 (m, 1H), 4.11 (q, 1H), 3.45 (s, 3H), 2.46 (s, 6H), 1.93-2.05 (m, 9H), 1.78-1.81 (m, 1H), 1.53-1.62 (m, 4H), 1.31 (d, 6H), 1.34-1.25 (m, 4H)
545	(400 MHz, $CDCl_3$) δ ppm 12.43 (s, 1H-NH), 10.11 (s, 1H-NH), 7.83 (s, 1H), 7.73 (br s, 2H), 7.49 (br s, 2H), 4.95-5.05 (m, 1H), 4.75-4.80 (m, 1H), 3.86-3.88 (m, 2H), 3.79-3.83 (m, 2H), 3.56-3.64 (m, 5H), 3.31-3.51 (m, 2H), 3.26 (s, 3H), 2.79 (br s, 6H), 2.27 (br s, 2H), 1.88-2.04 (m, 6H), 1.73-1.76 (m, 2H), 1.49-1.61 (m, 2H), 1.26 (d, 6H)
546	(400 MHz, $CDCl_3$) δ ppm 12.61 (s, 1H-NH), 10.06 (s, 1H-NH), 7.89 (s, 1H), 7.77 (br s, 2H), 7.51 (br s, 2H), 5.04 (br s, 1H), 4.77-4.02 (m, 1H), 3.48-3.83 (m, 7H), 3.06 (s, 6H), 2.82-2.98 (m, 5H), 2.20-2.44 (m, 2H), 1.91-2.01 (m, 6H), 1.75-1.79 (m, 2H), 1.52-1.58 (m, 2H), 1.21-1.36 (m, 1H), 1.29 (d, 6H)

Cpd Number	^{1}H NMR data
548	(400 MHz, $CDCl_3$) δ ppm 12.50 (br s, 1H-NH), 9.93 (br s, 1H-NH), 7.94-7.99 (m, 2H), 7.45 (s, 1H), 7.22-7.28 (m, 2H), 3.86-3.95 (m, 1H), 3.82 (d, 2H), 3.66 (br s, 1H), 3.41 (s, 3H), 3.36 (s, 3H), 3.35 (d, 2H), 3.13-3.28 (m, 3H), 3.03 (t, 2H), 2.57-2.67 (m, 4H), 2.41-2.55 (m, 4H), 2.05-2.21 (m, 6H).
549	(400 MHz, $CDCl_3$) δ ppm 8.08 (m, 2 H), 7.56 – 7.62 (m, 2H), 7.47 (s, 1 H), 7.36 – 7.42 (m, 1 H), 3.95 – 4.05 (m, 1 H), 3.73 – 3.77 (m, 2 H), 3.08 (s, 6 H), 2.93 – 3.01 (m, 2 H), 2.86 (br. s, 8 H), 2.60 – 2.72 (m, 3 H), 2.40 – 2.48 (m, 2 H), 2.06 – 2.18 (m, 4 H), 1.85 – 1.97 (m, 2 H), 1.74 – 1.81 (m, 1 H), 0.54 – 0.56 (m, 4 H)
551	(400 MHz, DMSO-d_6) δ ppm 11.71 (s, 1H), 10.97 (br s, 1H), 8.35 (d, 1H), 7.89-7.86 (m, 1H), 7.61 (s, 1H), 7.15 (d, 1H), 5.22-5.12 (m, 1H), 4.57-4.50 (m, 2H), 3.69-3.50 (m, 4H), 3.40-3.32 (m, 2H), 3.17-3.07 (m, 2H), 2.95 (s, 6H), 2.82 (m, 3H), 2.25-2.15 (m, 2H), 2.01-1.73 (m, 10H), 1.63-1.50 (m, 2H), 1.41-1.27 (m, 1H)
552	(400 MHz, DMSO-d_6) δ ppm 11.71 (s, 1H), 10.88 (br s, 1H), 8.34 (d, 1H), 7.90-7.86 (m, 1H), 7.61 (s, 1H), 7.15 (d, 1H), 5.22-5.13 (m, 1H), 4.55-4.48 (m, 2H), 3.79-3.76 (m, 2H), 3.64-3.56 (m, 3H), 3.49-3.32 (m, 6H), 3.21-3.11 (m, 2H), 2.94 (s, 6H), 2.25-2.15 (m, 2H), 2.04-1.71 (m, 10H), 1.63-1.50 (m, 2H), 1.38-1.27 (m, 1H)
553	(400 MHz, DMSO-d_6) δ ppm 12.9 (br s, 1H), 11.75 (br s, 1H), 11.44 (br s, 1H), 7.17 (s, 1H), 5.11-5.03 (m, 1H), 3.98-3.47 (m, 14H), 2.98-2.88 (m, 8H), 2.52-2.50 (m, 1H), 2.47-2.20 (m, 5H), 2.10-1.84 (m, 8H), 1.77-1.70 (m, 1H), 1.60-1.47 (m, 2H), 1.39-1.21 (m, 6H)

Cpd Number	^{1}H NMR data
554	(300 MHz, $CDCl_3$) δ ppm 7.87 (dd, *J*=8.5, 1.2 Hz, 2 H), 7.31 - 7.42 (m, 2 H), 7.24 (s, 1 H), 7.13 - 7.20 (m, 1 H), 3.78 (t, *J*=8.4 Hz, 1 H), 3.52 (d, *J*=12.0 Hz, 2 H), 3.05 - 3.22 (m, 2 H), 2.83 (s, 3 H), 2.71 - 2.78 (m, 2 H), 2.64 (br. s., 5 H), 2.35 - 2.51 (m, 3 H), 2.03 - 2.30 (m, 6 H), 1.81 - 2.01 (m, 4 H), 1.61 - 1.76 (m, 2 H), 1.40 - 1.58 (m, 3 H), 0.75 (t, *J*=7.3 Hz, 3 H), 0.33 (d, *J*=5.3 Hz, 4 H)
555	(300 MHz, $CDCl_3$) δ ppm 8.04 – 8.06 (m, 2 H), 7.53 – 7.59 (m, 2 H), 7.43 (s, 1 H), 7.33 – 7.38 (t, 1 H), 3.91 – 4.02 (m, 1 H), 3.69 – 3.79 (m., 6 H), 3.47 – 3.51 (m, 4 H), 2.90 – 2.99 (m., 2 H), 2.79 (br. s, 7 H), 2.58 – 2.66 (m, 4 H), 2.36 – 2.45 (m, 7 H), 2.03 – 2.15 (m, 4 H), 1.81 – 1.92 (m, 2 H), 1.69 – 1.75 (m, 1 H)
556	(300 MHz, $CDCl_3$) δ ppm 8.04 (dd, *J*=8.5, 1.2 Hz, 2 H), 7.51 - 7.63 (m, 2 H), 7.46 (s, 1 H), 7.32 - 7.42 (m, 1 H), 3.97 (quin, *J*=8.3 Hz, 2 H), 3.74 (d, *J*=12.3 Hz, 3 H), 3.41 (s, 3 H), 2.87 - 3.05 (m, 9 H), 2.77 (t, *J*=11.4 Hz, 1 H), 2.55 - 2.69 (m, 2 H), 2.35 - 2.51 (m, 2 H), 2.02 - 2.21 (m, 4 H), 1.70 - 1.97 (m, 3 H), 054 – 0.56 (m, 4 H)
557	(300 MHz, $CDCl_3$) δ ppm 8.08 (dd, *J*=8.7, 1.3 Hz, 2 H), 7.57 (t, *J*=7.9 Hz, 2 H), 7.46 (s, 1 H), 7.37 (s, 1 H), 2.96 (s, 3 H), 2.82 (br. s., 7 H), 2.51 - 2.69 (m, 6 H), 2.11 (br. s., 4 H), 1.83 (d, *J*=1.5 Hz, 4 H), 1.59 (s, 3 H), 1.43 (s, 4 H), 0.97 (d, *J*=1.8 Hz, 2 H), 0.52 (d, *J*=5.0 Hz, 4 H)
558	(300 MHz, $CDCl_3$) δ ppm 7.94 - 8.04 (m, 2 H), 7.58 (t, *J*=7.9 Hz, 2 H), 7.49 (s, 1 H), 7.34 - 7.44 (m, 1 H), 4.01 (t, *J*=8.5 Hz, 1 H), 3.71 (d, *J*=12.0 Hz, 2 H), 2.94 (t, *J*=11.9 Hz, 6 H), 2.74 (s, 6 H), 2.59 – 2.70 (m, 3 H), 2.42 (dd, *J*=8.2, 4.7 Hz, 4 H), 1.98 - 2.17 (m, 4 H), 1.74 - 1.91 (m, 2 H), 1.65 (dq, *J*=6.8, 3.3 Hz, 1 H), 1.37 - 1.48 (m, 5 H)

Cpd Number	^{1}H NMR data
559	(400 MHz, $CDCl_3$) δ ppm 13.2 (1H, s), 9.98 (1H, s), 7.77(3H, m), 7.60 (2H, d), 5.01 (1H, m), 4.73(1H, m), 4.42 (2H,t), 4.01 (2H, m), 3.69 (3H, d), 3.02 (6H, s), 2.56 (1H, s), 1.90(6H, m), 1.73(1H, d), 1.57(3H, m), 1.25 (7H, m), 0.94 (1H, m)
560	(400 MHz, $CDCl_3$) δ ppm 13.74 (br. s., 1 H), 9.90 (s, 1 H), 7.85 - 8.11 (m, 2 H), 7.46 (s, 1 H), 7.11 - 7.34 (m, 2 H), 4.12 (br. s., 1 H), 3.88 - 4.02 (m, 2 H), 3.81 (d, *J*=12.5 Hz, 2 H), 3.50 (br. s., 1 H), 3.23 (br. s., 1 H), 3.06 (s, 8 H), 2.96 (t, *J*=12.1 Hz, 2 H), 2.68 - 2.80 (m, 1 H), 2.55 - 2.67 (m, 3 H), 2.42 - 2.54 (m, 3 H), 2.34 (br. s., 3 H), 2.15 - 2.25 (m, 1 H), 2.00 - 2.13 (m, 1 H), 1.64 - 1.69 (m, 2H)
561	(400 MHz, $CDCl_3$) δ ppm 9.89 (br. s., 1 H), 8.01 (br. s., 2 H), 7.47 (br. s., 1 H), 4.19 (br. s., 1 H), 3.90 - 4.06 (m, 2 H), 3.63 - 3.89 (m, 3 H), 3.28 (br. s., 3 H), 3.06 (s, 3 H), 2.85 – 3.05 (m, 2 H), 2.83 (br.s., 1 H), 2.31 - 2.73 (m, 9 H), 1.99 - 2.31 (m, 3 H), 1.28 (br.s, 3 H)
562	(HCl salt) (400 MHz, $CDCl_3$) δ ppm 13.52 (br. s., 1 H), 9.89 (br. s., 1 H), 8.01 (br. s., 2 H), 7.47 (br. s., 1 H), 7.28 (br. s., 2 H), 4.06 (br. s., 1 H), 3.86 (br. s., 3 H), 3.55 - 3.74 (m, 1 H), 3.41 (br. s., 1 H), 3.06 (br. s., 8 H), 2.80 - 2.91 (m, 1 H), 2.38 - 2.77 (m, 6 H), 2.01 - 2.33 (m, 4 H), 1.82 (br. s., 1 H), 1.63 (br. s., 3 H), 1.28 (br. s., 2 H)

Cpd Number	^{1}H NMR data
563	(HCl salt) (400 MHz, $CDCl_3$) δ ppm 13.23 (br. s., 1 H), 9.73 - 10.01 (m, 1 H), 8.02 (d, *J*=4.6 Hz, 2 H), 7.47 (br. s., 1 H), 7.28 (s, 1H), 4.42 (br. s., 1 H), 4.02 (d, *J*=8.3 Hz, 1 H), 3.93 (d, *J*=7.8 Hz, 1 H), 3.85 (d, *J*=9.5 Hz, 2 H), 3.72 (br. s., 1 H), 3.59 (br. s., 1 H), 3.54 (br. s., 1 H), 3.46 (br. s., 1 H), 3.07 (s, 6 H), 2.98 (d, *J*=13.7 Hz, 2 H), 2.83 (s, 3 H), 2.57 - 2.70 (m, 2 H), 2.48 (br. s., 4 H), 2.27 (br. s., 2 H), 2.18 (br. s., 1 H), 2.11 (br. s., 2 H), 2.03 (s, 1 H)
564	(400 MHz, $CDCl_3$) δ ppm 7.83 - 8.10 (m, 2 H), 7.38 - 7.55 (m, 1 H), 7.22 - 7.35 (m, 2 H), 4.12 (br. s., 1 H), 3.91 - 4.03 (m, 2 H), 3.83 (d, *J*=12.2 Hz, 2 H), 3.50 (d, *J*=9.3 Hz, 1 H), 3.43 (s, 3 H), 3.24 (d, *J*=12.5 Hz, 1 H), 2.91 - 3.11 (m, 4 H), 2.69 - 2.82 (m, 1 H), 2.42 - 2.68 (m, 6 H), 2.27 - 2.40 (m, 3 H), 2.16 - 2.27 (m, 1 H), 2.01 - 2.15 (m, 1 H)
565	(400 MHz, $CDCl_3$) δ ppm 13.83 (br. s., 1 H), 9.96 (br. s., 1 H), 7.83 - 8.09 (m, 2 H), 7.42 - 7.54 (m, 1 H), 7.18 - 7.34 (m, 2 H), 3.89 - 4.10 (m, 2 H), 3.82 (d, *J*=10.0 Hz, 2 H), 3.43 (s, 3 H), 3.22 - 3.39 (m, 2 H), 2.94 - 3.11 (m, 2 H), 2.83 (br. s., 1 H), 2.61 (dt, *J*=18.2, 9.2 Hz, 2 H), 2.30 - 2.54 (m, 6 H), 2.00 - 2.26 (m, 3 H), 1.54 - 1.76 (m, 3 H)
566	(300 MHz, $CDCl_3$-*d*) δ ppm 7.87 (dd, *J*=9.0, 4.6 Hz, 2 H), 7.27 - 7.45 (m, 1 H), 7.04 - 7.25 (m, 2 H), 3.95 (br. s., 1 H), 3.66 - 3.90 (m, 3 H), 3.55 (br. s., 1 H), 3.34 (s, 3 H), 2.95 (br. s., 2 H), 2.81 (br. s., 1 H), 2.43 - 2.65 (m, 4 H), 2.39 (br. s., 4 H), 2.20 (s, 1 H), 1.89 - 2.15 (m, 5 H), 1.74 (d, *J*=9.9 Hz, 1 H), 1.55 (d, *J*=19.4 Hz, 2 H)

Cpd Number	^{1}H NMR data
567	(HCl salt) (300 MHz, $CDCl_3$) δ ppm 13.18 (br. s., 1 H), 9.87 (br. s., 1 H), 7.87 - 7.90 (dd, *J*=9.2, 4.8 Hz, 2 H), 7.22 - 7.39 (d, *J*=3.3 Hz, 1 H), 7.04 - 7.28 (m, 2 H), 3.60 - 4.01 (m, 4 H), 3.41 - 3.53 (m, 2 H), 3.34 (s, 3 H), 2.76 - 3.14 (m, 4 H), 1.90 - 2.67 (m, 13 H), 1.64 - 1.84 (m, 2 H)
568	(400 MHz, $CDCl_3$) δ ppm 7.90 - 8.10 (m, 2 H), 7.42 - 7.52 (m, 1 H), 7.14 - 7.33 (m, 2 H), 3.91 - 4.09 (m, 1 H), 3.77 - 3.86 (m, 4 H), 3.72 (d, *J*=12.7 Hz, 2 H), 3.32 - 3.51 (m, 4 H), 2.96 (t, *J*=11.5 Hz, 2 H), 2.55 - 2.70 (m, 6 H), 2.33 - 2.50 (m, 3 H), 2.00 - 2.19 (m, 4 H), 1.81 (qd, *J*=11.9, 3.5 Hz, 2 H), 1.43 - 1.75 (m, 7 H)
569	(400 MHz, $CDCl_3$) δ ppm 7.92 - 8.05 (m, 2 H), 7.50 (s, 1 H), 7.18 - 7.33 (m, 2 H), 4.34 - 4.58 (m, 4 H), 4.01 (quin, *J*=8.2 Hz, 1 H), 3.78 - 3.86 (m, 4 H), 3.74 (d, *J*=12.7 Hz, 2 H), 2.99 (t, *J*=11.6 Hz, 2 H), 2.55 - 2.73 (m, 6 H), 2.35 - 2.50 (m, 3 H), 2.00 - 2.20 (m, 4 H), 1.82 (qd, *J*=11.9, 3.4 Hz, 3 H)
570	(400 MHz, $CDCl_3$) δ ppm 13.19 (br. s., 1 H), 9.89 (br. s., 1 H), 8.00 (br. s., 2 H), 7.46 (br. s., 1 H), 7.28 (br. s., 2 H), 4.35 - 4.76 (m, 3 H), 3.61 - 4.09 (m, 6 H), 3.38 (br. s., 3 H), 2.82 - 3.27 (m, 8 H), 2.39 - 2.71 (m, 4 H), 1.97 - 2.33 (m, 6 H)
571	(HCl salt) (400 MHz, $CDCl_3$) δ ppm 13.09 (br. s., 1 H), 9.89 (br. s., 1 H), 7.85 - 8.07 (m, 2 H), 7.45 (br. s., 1 H), 7.16 - 7.33 (m, 2 H), 4.62 (br. s., 1 H), 3.88 - 4.01 (m, 1 H), 3.84 (d, *J*=8.6 Hz, 2 H), 3.70 (br. s., 2 H), 3.52 (br. s., 2 H), 3.06 (s, 6 H), 2.82 (s, 6 H), 2.61 (d, *J*=8.1 Hz, 3 H), 2.47 (br. s., 3 H), 2.02 - 2.31 (m, 4 H), 1.71 (br. s., 1 H)

Cpd Number	^{1}H NMR data
572	(400 MHz, $CDCl_3$) δ ppm 12.89 (br. s, 1 H), 9.89 (s, 1 H), 8.01 (br. s, 2 H), 7.45 (s, 1 H), 7.29 (m, 2 H), 4.15 (br. s, 1 H), 3.78 – 3.93 (m, 3 H), 3.37 – 3.62 (m, 7 H), 3.05 (br. s, 8 H), 2.79 (br. s, 1 H), 2.47 – 2.64 (m, 8 H), 2.05 – 2.18 (m, 6 H)
573	(300 MHz, $CDCl_3$) δ ppm 12.58 (br. s., 1 H), 9.81 (s, 1 H), 7.91 (dd, *J*=8.8, 4.8 Hz, 2 H), 7.37 (s, 1 H), 7.02 - 7.28 (m, 2 H), 4.39 (br. s., 2 H), 3.70 - 3.96 (m, 4 H), 3.45 (br. s., 1 H), 3.23 (br. s., 1 H), 2.98 (s, 6 H), 2.74 (s, 3 H), 2.17 - 2.62 (m, 6 H), 1.90 - 2.15 (m, 2 H), 1.73 (br. s., 5 H), 1.55 (br. s., 2 H), 1.25 - 1.40 (m, 2 H), 1.18 (br. s., 1 H)
575	(400 MHz, $CDCl_3$) δ ppm 9.80 (br. s., 1 H), 8.36 – 8.38 (d, 1 H), 8.16 – 8.19 (m, 1 H), 7.82 – 7.85 (m, 1 H), 7.56 - 7.58 (m, 1 H), 7.29 – 7.33 (m, 1 H), 4.33 – 4.55 (br. s., 2 H), 4.01 – 4.17 (br. s, 2 H), 3.92 – 3.98 (m, 1 H), 3.80 – 3.84 (m, 2 H), 3.46 – 3.60 (br. s, 1H), 3.29 (br. s, 1 H), 3.11 (s., 6 H), 3.01 – 3.11 (m, 1 H), 2.22 – 2.68 (m, 8 H), 1.60 – 1.76 (br. s., 3 H), 1.47 (s, 1 H), 1.29 (br. s, 3H)
576	(400 MHz, $CDCl_3$) δ ppm 9.76 - 10.08 (m, 1 H), 7.92 - 8.09 (m, 2 H), 7.51 (s, 1 H), 7.16 - 7.32 (m, 2 H), 4.27 (t, *J*=7.7 Hz, 3 H), 3.94 - 4.12 (m, 1 H), 3.78 - 3.87 (m, 4 H), 3.74 (d, *J*=12.7 Hz, 2 H), 2.98 (t, *J*=11.4 Hz, 2 H), 2.56 - 2.72 (m, 6 H), 2.37 - 2.50 (m, 3 H), 2.29 (quin, *J*=7.7 Hz, 2 H), 1.99 - 2.18 (m, 4 H), 1.82 (qd, *J*=12.0, 3.4 Hz, 3 H)

Cpd Number	^{1}H NMR data
579	(400 MHz, $CDCl_3$) δ ppm 8.00 – 8.04 (m, 2 H), 7.44 (s, 1 H), 7.26 – 7.29 (m, 2 H), 4.15 – 4.22 (m, 1 H), 3.97 – 4.04 (m, 3 H), 3.78 – 3.83 (m, 4 H), 3.71 - 3.74 (m, 2 H), 3.46 – 3.52 (m, 2 H), 2.94 – 2.99 (m, 2 H), 3.00 (s, 3 H), 2.59 – 2.67 (m, 6 H), 2.38 – 2.45 (m, 3 H), 2.06 – 2.14 (m, 4 H), 1.73 – 1.87 (m, 7 H)
580	(300 MHz, $CDCl_3$) δ ppm 7.87 - 8.12 (m, 2 H), 7.51 (s, 1 H), 7.15 - 7.39 (m, 2 H), 4.63 (t, *J*=12.0 Hz, 3 H), 4.02 (t, *J*=8.3 Hz, 1 H), 3.65 - 3.90 (m, 6 H), 3.01 (t, *J*=11.6 Hz, 2 H), 2.56 - 2.79 (m, 7 H), 2.46 (dd, *J*=8.0, 4.1 Hz, 3 H), 2.00 - 2.28 (m, 4 H), 1.70 - 1.96 (m, 2 H)
583	(400 MHz, DMSO-d_6) δ ppm 11.48 (s, 1H), 8.37-8.32 (m, 2H), 7.45-7.38 (m, 2H), 7.26 (s, 1H), 4.01-3.93 (m, 1H), 3.74-3.67 (m, 3H), 3.-60-3.32 (m, 9H), 3.2-2.96 (m, 2H), 2.92 (s, 6H), 2.49-2.39 (m, 4H), 2.37-2.25 (m, 2H), 2.16-1.94 (m, 4H), 1.01-0.61 (m, 4H)
584	(400 MHz, $CDCl_3$) δ ppm 12.07 (br s, 1H), 9.82 (br s, 1H), 7.97-7.91 (m, 2H), 7.40 (s, 1H), 7.21-7.15 (m, 2H), 3.90-3.80 (m, 1H), 3.57-3.48 (m, 2H), 3.41-3.32 (m, 1H), 3.26-3.18 (m, 3H), 3.02-2.88 (m, 8H), 2.59-2.46 (m, 2H), 2.42-2.27 (m, 5H), 2.05-1.96 (m, 2H), 1.89-1.70 (m, 6H), 1.58-1.53 (m, 2H), 0.85-0.78 (m, 2H)
585	(400 MHz, $CDCl_3$) δ ppm 7.94 – 7.98 (m, 2 H), 7.47 (s, 1 H), 7.22 – 7.28 (m, 2 H), 4.38 – 4.57 (m, 3 H), 3.87 – 3.98 (m, 1 H), 3.75 – 3.80 (m, 2 H), 3.57 – 3.70 (br. s, 2 H), 3.41 (s, 3 H), 3.35 (s, 3 H), 3.05 – 3.17 (br. s, 1 H), 2.91 – 2.99 (m, 2 H), 2.52 – 2.62 (m, 2 H), 2.40 – 2.49 (m, 2 H), 2.01 – 2.26 (m, 7 H)

Cpd Number	^{1}H NMR data
586	(300 MHz, $CDCl_3$) δ ppm 7.71 - 7.97 (m, 2 H), 7.37 (s, 1 H), 7.00 - 7.22 (m, 2 H), 3.69 - 3.97 (m, 3 H), 3.43 - 3.67 (m, 3 H), 3.34 (s, 4 H), 2.96 (t, *J*=11.6 Hz, 2 H), 2.29 - 2.85 (m, 8 H), 1.81 - 2.26 (m, 6 H), 1.18 (br. s., 2 H)
587	(400 MHz, $CDCl_3$) δ ppm 12.90 (br. s., 1 H), 9.95 (br. s., 1 H), 7.98 (dd, *J*=8.8, 4.6 Hz, 2 H), 7.47 (s, 1 H), 7.18 - 7.38 (m, 2 H), 4.16 (br. s., 1 H), 3.88 - 3.98 (m, 1 H), 3.84 (d, *J*=12.2 Hz, 2 H), 3.63 (d, *J*=7.8 Hz, 1 H), 3.52 (br. s., 1 H), 3.48 (s, 3 H), 3.43 (s, 3 H), 3.38 (br. s., 1 H), 3.04 (t, *J*=11.7 Hz, 2 H), 2.78 (br. s., 1 H), 2.50 - 2.67 (m, 5 H), 2.47 (br. s., 2 H), 2.41 (br. s., 2 H), 2.09 - 2.26 (m, 4 H), 1.97 - 2.09 (m, 2 H)
588	(400 MHz, $CDCl_3$) δ ppm 7.98 (br. s., 2 H), 7.45 (br. s., 1 H), 7.28 (br. s., 2 H), 4.48 (t, *J*=11.6 Hz, 1 H), 3.72 - 4.07 (m, 4 H), 3.54 (d, *J*=11.2 Hz, 1 H), 3.22 - 3.46 (m, 5 H), 2.85 - 3.19 (m, 4 H), 1.99 - 2.76 (m, 6 H), 1.82 (br. s., 3 H), 1.66 (br. s., 3 H), 1.10 - 1.51 (m, 5 H)
589	(400 MHz, DMSO-d_6) δ ppm 11.52 (br s, 1H), 10.12 (br s, 1H), 8.38-8.32 (m, 2H), 7.46-7.39 (m, 2H), 7.24 (s, 1H), 4.01-3.91 (m, 1H), 3.67-3.56 (m, 5H), 3.21-3.16 (m, 2H), 3.01-2.86 (m, 10H), 2.51-2.37 (m, 3H), 2.12-1.86 (m, 9H), 1.59-1.47 (m, 2H)
590	(400 MHz, $CDCl_3$) δ ppm 9.88 (s, 1 H), 7.88 - 8.08 (m, 2 H), 7.39 - 7.54 (m, 1 H), 7.12 - 7.34 (m, 1 H), 4.12 - 4.46 (m, 4 H), 3.74 - 3.99 (m, 5 H), 3.47 - 3.65 (m, 2 H), 3.24 - 3.40 (m, 1 H), 2.81 - 3.14 (m, 10 H), 2.63 (t, *J*=8.7 Hz, 2 H), 2.47 (br. s., 4 H), 2.00 - 2.33 (m, 5 H) , 1.77 (m, 2 H)

Cpd Number	^{1}H NMR data
591	(400 MHz, $CDCl_3$) δ ppm 12.81 - 13.07 (m, 1 H), 9.89 (s, 1 H), 8.01 (dd, *J*=8.9, 4.8 Hz, 2 H), 7.47 (s, 1 H), 7.17 - 7.33 (m, 2 H), 4.04 (br. s., 2 H), 3.87 - 3.98 (m, 1 H), 3.75 - 3.86 (m, 2 H), 3.51 - 3.64 (m, 1 H), 3.44 (s, 4 H), 3.25 - 3.33 (m, 1 H), 3.07 (s, 8 H), 2.90 (d, *J*=2.9 Hz, 3 H), 2.63 (br. s., 3 H), 2.35 - 2.50 (m, 3 H), 1.98 - 2.21 (m, 3 H)
592	(400 MHz, $CDCl_3$) δ ppm 7.82 - 8.02 (m, 2 H), 7.49 - 7.66 (m, 1 H), 7.10 - 7.38 (m, 2 H), 4.02 (t, *J*=8.4 Hz, 1 H), 3.77 - 3.88 (m, 7 H), 3.70 (d, *J*=12.4 Hz, 2 H), 2.85 - 3.00 (m, 2 H), 2.53 - 2.79 (m, 6 H), 2.32 - 2.47 (m, 4 H), 1.92 - 2.22 (m, 5 H), 1.68 - 1.88 (m, 2 H)
593	(400 MHz, $CDCl_3$) δ ppm 8.06 (s, 1 H), 7.99 - 8.04 (m, 2 H), 7.24 - 7.32 (m, 2 H), 3.99 (t, *J*=8.3 Hz, 1 H), 3.44 (s, 3 H), 3.21 (d, *J*=9.6 Hz, 3 H), 2.60 - 2.73 (m, 3 H), 2.51 (td, *J*=8.4, 3.8 Hz, 4 H), 2.16 - 2.29 (m, 4 H), 1.89 - 2.14 (m, 7 H), 1.70 - 1.88 (m, 3 H)
594	(400 MHz, $CDCl_3$) δ ppm 8.02 – 8.06 (m, 3 H), 7.26 – 7.30 (m, 2 H), 3.95 – 4.03 (m, 1 H), 3.15 – 3.24 (m, 3 H), 3.06 (s, 6 H), 2.59 – 2.70 (m, 3 H), 2.44 – 2.53 (m, 4 H), 2.16 – 2.26 (m, 3 H), 1.88 – 2.11 (m, 8 H), 1.70 – 1.83 (m, 4 H)
598	(400 MHz, $CDCl_3$) δ ppm 7.92 - 8.12 (m, 3 H), 7.13 - 7.38 (m, 2 H), 3.97 (t, *J*=8.3 Hz, 1 H), 3.45 (d, *J*=11.8 Hz, 2 H), 3.21 - 3.35 (m, 2 H), 3.07 (s, 5 H), 2.58 - 2.75 (m, 4 H), 2.43 - 2.53 (m, 2 H), 2.18 - 2.39 (m, 3 H), 1.94 - 2.13 (m, 3 H), 1.30 (d, *J*=6.7 Hz, 6 H)

Cpd Number	^{1}H NMR data
599	(400 MHz, DMSO-d_6) δ ppm 8.37 - 8.48 (m, 2 H), 7.92 (s, 1 H), 7.29 - 7.47 (m, 2 H), 4.12 (t, *J*=8.3 Hz, 1 H), 4.00 (dd, *J*=11.1, 3.6 Hz, 2 H), 3.55 (d, *J*=11.1 Hz, 2 H), 3.15 (dd, *J*=10.0, 5.2 Hz, 3 H), 2.97 (s, 4 H), 2.46 – 2.56 (m, 5 H), 1.89 - 2.24 (m, 8 H), 1.69 (dd, *J*=11.9, 3.8 Hz, 3 H)
600	(400 MHz, $CDCl_3$) δ ppm 7.92 - 8.05 (m, 2 H), 7.19 - 7.36 (m, 3 H), 3.89 - 4.08 (m, 2 H), 3.36 - 3.48 (m, 4 H), 3.09 - 3.31 (m, 3 H), 2.58 - 2.73 (m, 4 H), 2.45 - 2.55 (m, 2 H), 2.38 (d, *J*=7.2 Hz, 2 H), 2.14 - 2.28 (m, 3 H), 1.98 - 2.13 (m, 3 H), 1.82 - 1.92 (m, 3 H), 1.74 (d, *J*=13.1 Hz, 2 H), 1.34 (qd, *J*=12.3, 4.4 Hz, 2 H)
601	(400 MHz, $CDCl_3$) δ ppm 7.90 - 8.15 (m, 2 H), 7.22 - 7.39 (m, 3 H), 3.85 - 4.13 (m, 3 H), 3.35 - 3.55 (m, 2 H), 3.18 - 3.33 (m, 3 H), 3.01 - 3.09 (m, 6 H), 2.54 - 2.76 (m, 3 H), 2.41 - 2.52 (m, 3 H), 2.34 (t, *J*=11.2 Hz, 2 H), 2.01 - 2.25 (m, 4 H), 1.83 - 1.99 (m, 3 H), 1.75 (d, *J*=13.0 Hz, 2 H), 1.23 - 1.52 (m, 2 H)
602	(400 MHz, $CDCl_3$) δ ppm 7.85 - 8.11 (m, 2 H), 7.09 - 7.42 (m, 3 H), 3.85 - 4.11 (m, 1 H), 3.32 - 3.57 (m, 8 H), 2.98 - 3.28 (m, 3 H), 2.29 - 2.73 (m, 10 H), 1.62 - 2.25 (m, 12 H)
603	(400 MHz, $CDCl_3$) δ ppm 8.03 (s, 1 H), 8.00 – 8.02 (m, 1 H), 7.26 – 7.31 (m, 3 H), 3.95 – 4.03 (m, 1 H), 3.45 (s, 3 H), 3.20 – 3.28 (m, 1 H), 3.16 – 3.19 (m, 2 H), 2.66 – 2.77 (m, 3 H), 2.64 (s, 2 H), 2.35 – 2.54 (m, 3 H), 1.90 – 2.31 (m, 9 H)

Cpd Number	^{1}H NMR data
604	(400 MHz, $CDCl_3$) δ ppm 9.76 - 9.97 (m, 1 H), 7.95 - 8.09 (m, 3 H), 7.18 - 7.35 (m, 2 H), 3.98 (quin, *J*=8.4 Hz, 1 H), 3.13 - 3.30 (m, 3 H), 3.07 (s, 6 H), 2.60 - 2.80 (m, 4 H), 2.36 - 2.57 (m, 6 H), 2.14 - 2.33 (m, 3 H), 1.85 - 2.12 (m, 3 H)
605	(400 MHz, $CDCl_3$) δ ppm 11.81 (br s, 1H-NH), 9.91 (br s, 1H-NH), 7.94-7.99 (m, 2H), 7.43 (s, 1H), 7.20-7.26 (m, 2H), 4.28 (br s, 1H), 3.74-3.94 (m, 3H), 3.25-3.45 (m, 5H), 3.02 (s, 6H), 2.97-3.09 (m, 3H), 2.39-2.62 (m, 8H), 1.99-2.21 (m, 6H)
606	(400 MHz, $CDCl_3$) δ ppm 8.05 (dd, *J*=8.8, 4.9 Hz, 1 H), 7.95 (d, *J*=7.3 Hz, 1 H), 7.00 (s, 1 H), 6.79 (t, *J*=8.7 Hz, 1 H), 6.47 (d, *J*=7.6 Hz, 1 H), 3.73 - 3.93 (m, 1 H), 3.67 - 3.72 (m, 2 H), 3.64 (s, 2 H), 3.47 - 3.58 (m, 3 H), 3.35 (d, *J*=12.0 Hz, 1 H), 2.73 - 2.92 (m, 3 H), 2.59 (t, *J*=11.5 Hz, 1 H), 2.26 - 2.46 (m, 4 H), 2.00 - 2.19 (m, 2 H), 1.67 - 1.93 (m, 3 H), 1.51 (d, *J*=8.8 Hz, 4 H)
606	(400 MHz, $CDCl_3$) δ ppm 8.05 (dd, *J*=8.8, 4.9 Hz, 1 H), 7.95 (d, *J*=7.3 Hz, 1 H), 7.00 (s, 1 H), 6.79 (t, *J*=8.7 Hz, 1 H), 6.47 (d, *J*=7.6 Hz, 1 H), 3.73 - 3.93 (m, 1 H), 3.67 - 3.72 (m, 2 H), 3.64 (s, 2 H), 3.47 - 3.58 (m, 4 H), 3.35 (d, *J*=12.0 Hz, 1 H), 2.73 - 2.92 (m, 3 H), 2.59 (t, *J*=11.5 Hz, 1 H), 2.26 - 2.46 (m, 4 H), 2.00 - 2.19 (m, 2 H), 1.67 - 1.93 (m, 3 H), 1.51 (d, *J*=8.8 Hz, 4 H)
607	(400 MHz, $CDCl_3$) δ ppm 13.99 (br s, 1H), 13.77 (br s, 1H), 9.86 (br s, 1H), 8.04-7.97 (m, 2H), 7.45 (s, 1H), 7.28-7.21 (m, 2H), 4.39-4.15 (m, 4H), 3.95-3.75 (m, 7H), 3.56-3.46 (m, 3H), 3.45-3.18 (m, 6H), 3.07-2.91 (m, 7H), 2.64-2.34 (m, 6H), 2.32-2.00 (m, 4H)

Cpd Number	^{1}H NMR data
608	(300 MHz, $CDCl_3$) δ ppm 7.96 - 8.12 (m, 3 H), 7.47 (s, 1 H), 7.19 - 7.34 (m, 1 H), 3.86 - 4.09 (m, 3 H), 3.66 - 3.81 (m, 5 H), 3.57 (td, *J*=9.9, 7.0 Hz, 1 H), 3.36 - 3.49 (m, 6 H), 2.91 - 3.19 (m, 3 H), 2.67 - 2.76 (m, 3 H), 2.55 - 2.65 (m, 4 H), 2.37 - 2.52 (m, 2 H), 1.85 - 2.30 (m, 7 H), 1.48 - 1.73 (m, 2 H)
610	(400 MHz, $CDCl_3$) δ ppm 7.95 - 8.08 (m, 2 H), 7.44 (s, 1 H), 7.22 - 7.24 (m, 2 H), 3.99 (t, *J*=8.4 Hz, 1 H), 3.69 (d, *J*=12.5 Hz, 2 H), 3.58 - 3.63 (m, 4 H), 3.56 (t, *J*=5.2 Hz, 2 H), 3.42 (s, 3 H), 3.39 (d, *J*=6.3 Hz, 2 H), 3.34 (s, 3 H), 2.92 - 3.01 (m, 2 H), 2.75 (dt, *J*=10.4, 5.1 Hz, 6 H), 2.56 - 2.65 (m, 2 H), 2.39 - 2.49 (m, 2 H), 2.02 - 2.16 (m, 2 H), 1.85 - 2.00 (m, 3 H), 1.51 - 1.64 (m, 2 H)
614	(400 MHz, DMSO-d_6) δ ppm 8.39-8.34 (m, 2H), 7.43-7.37 (m, 2H), 7.26 (s, 1H), 4.56-4.52 (m, 2H), 4.46-4.43 (m, 2H), 4.01-3.93 (m, 1H), 3.51-3.43 (m, 1H), 3.26-3.19 (m, 4H), 2.86 (s, 6H), 2.50-2.36 (m, 4H), 2.33-2.26 (m, 4H), 2.11-1.94 (m, 2H), 1.72-1.65 (m, 4H), 1.62-1.56 (m, 4H)
615	(400 MHz, DMSO-d_6) δ ppm 8.39-8.35 (m, 2H), 7.43-7.37 (m, 2H), 7.25 (s, 1H), 4.56-4.53 (m, 2H), 4.45-4.42 (m, 2H), 4.02-3.93 (m, 1H), 3.66-3.58 (m, 2H), 3.45-3.39 (m, 2H), 2.98-2.90 (m, 2H), 2.86 (s, 6H), 2.82-2.54 (m, 5H), 2.49-2.27 (m, 7H), 2.13-1.93 (m, 4H), 1.79-1.67 (m, 2H)
616	(400 MHz, DMSO-d_6) δ ppm 11.65 (1H, s), 10.30 (1H, s), 8.35 (2H, m), 7.42 (3H, m), 4.29 (2H, d), 4.06 (1H, m), 3.57 (2H, m), 3.24 (1H, m), 2.93 (6H, s), 2.76 (1H, m), 2.45 (4H, m), 2.23 (1H, m), 2.14 (1H, m), 2.03 (2H, d), 1.93 (1H, m), 1.74 (2H, m), 1.25 (1H, m), 1.11 (

Cpd Number	^{1}H NMR data
617	(400 MHz, DMSO-d_6) δ ppm 11.66 (1H, s), 10.69 (1H, s), 8.34 (2H, m), 7.41 (3H, m), 4.29 (2H, d), 4.05 (1H, m), 3.56 (1H, m), 3.41 (2H, d), 2.93 (6H, s), 2.81 (2H, m), 2.44 (6H, m), 2.17 (4H, m), 2.03 (2H, d), 1.94 (1H, m), 1.75 (4H, m)
618	(400 MHz, DMSO-d_6) δ ppm 11.61 (1H, s), 10.34 (1H, s), 8.34 (2H, m), 7.40 (3H, m), 4.27(2H, d) 4.05 (1H, m), 3.46 (2H, d), 3.10 (3H, m), 2.93 (6H, s), 2.43 (4H, m), 2.23 (1H, m), 2.12 (3H, m), 2.03(2H, d), 1.87 (5H, m), 1.61 (1H, d), 1.44 (2H, m), 1.28 (2H, m), 1.10 (1H, m)
619	(400 MHz, DMSO-d_6) δ ppm 11.64 (1H, s), 10.26 (1H, s), 8.35 (2H, m), 7.42 (3H, m), 4.29(2H, d), 4.05 (1H, m), 3.98 (2H, m), 3.57 (2H, m), 3.35 (2H, m), 3.04 (2H, m), 2.93(6H, s), 2.44 (4H, m), 2.24 (1H, s), 2.05 (5H, m), 1.94 (2H, m), 1.75 (4H, m)
620	(400 MHz, $CDCl_3$) δ ppm 7.87 - 8.13 (m, 3 H), 7.08 - 7.39 (m, 2 H), 3.78 - 4.08 (m, 1 H), 3.33 - 3.55 (m, 7 H), 3.12 - 3.26 (m, 2 H), 3.08 (s, 6 H), 2.54 - 2.83 (m, 4 H), 1.78 - 2.54 (m, 15 H)
623	(400 MHz, $CDCl_3$) δ ppm 13.57 (br. s., 1 H), 9.85 (s, 1 H), 7.79 - 7.86 (m, 2 H), 7.49 (s, 1 H), 7.24 - 7.29 (m, 1 H), 4.38 - 4.48 (m, 2 H), 4.06 – 4.12 (m, 2 H), 3.81 – 3.95 (m, 3 H), 3.49 – 3.57 (m, 2 H), 3.07 (s, 10 H), 2.83 (s, 2 H), 2.56 – 2.65 (m, 2 H), 2.42 – 2.53 (m, 3 H), 2.28 – 2.38 (m, 2 H), 2.07 – 2.20 (m, 2 H)

Cpd Number	^{1}H NMR data
625	(400 MHz, $CDCl_3$) δ ppm 8.48 (s, 1 H), 7.96 - 8.04 (m, 2 H), 7.46 (s, 1 H), 7.21 - 7.31 (m, 2 H), 3.91 (quin, J=8.3 Hz, 1 H), 3.70 - 3.83 (m, 2 H), 3.61 (dd, J=12.7, 4.0 Hz, 1 H), 3.39 - 3.52 (m, 2 H), 3.25 - 3.37 (m, 2 H), 3.01 - 3.13 (m, 7 H), 2.87 (br. s., 1 H), 2.52 - 2.69 (m, 2 H), 2.43 (dd, J=11.4, 7.0 Hz, 2 H), 1.99 - 2.27 (m, 6 H), 1.42 (t, J=6.8 Hz, 6 H)
626	(400 MHz, $CDCl_3$) δ ppm 9.74 - 10.01 (m, 1 H), 7.90 - 8.08 (m, 2 H), 7.45 (s, 1 H), 7.20 - 7.31 (m, 2 H), 3.86 - 4.00 (m, 1 H), 3.78 (d, *J*=13.5 Hz, 1 H), 3.64 (dd, *J*=12.5, 5.8 Hz, 1 H), 3.51 - 3.58 (m, 2 H), 3.45 (dd, *J*=12.8, 4.6 Hz, 2 H), 3.11 - 3.28 (m, 2 H), 3.00 - 3.10 (m, 6 H), 2.88 (br. s., 1 H), 2.55 - 2.73 (m, 5 H), 2.37 - 2.49 (m, 2 H), 1.94 - 2.32 (m, 9 H), 1.75 - 1.92 (m, 1 H)
627	(400 MHz, $CDCl_3$) δ ppm 9.93 (br. s., 1 H), 7.95 - 8.06 (m, 2 H), 7.46 (s, 1 H), 7.21 - 7.31 (m, 2 H), 4.78 - 4.92 (m, 3 H), 4.74 (t, *J*=6.8 Hz, 1 H), 4.07 (br. s., 1 H), 3.95 (quin, *J*=8.4 Hz, 1 H), 3.41 - 3.60 (m, 2 H), 3.26 - 3.40 (m, 3 H), 3.06 (s, 6 H), 2.93 (br. s., 1 H), 2.69 - 2.86 (m, 1 H), 2.65 - 2.69 (m, 2 H), 2.54 - 2.65 (m, 3 H), 2.34 - 2.49 (m, 2 H), 1.97 - 2.16 (m, 4 H)
628	(400 MHz, $CDCl_3$) δ ppm 7.90 - 8.09 (m, 2 H), 7.47 (s, 1 H), 7.12 - 7.32 (m, 2 H), 4.04 - 4.25 (m, 2 H), 3.93 (quin, *J*=8.2 Hz, 1 H), 3.67 - 3.81 (m, 2 H), 3.59 (dd, *J*=12.8, 4.6 Hz, 1 H), 3.34 - 3.52 (m, 4 H), 3.28 (br. s., 1 H), 3.01 - 3.19 (m, 8 H), 2.82 (br. s., 1 H), 2.53 - 2.73 (m, 4 H), 2.44 (dtt, *J*=11.7, 7.8, 7.8, 4.0, 4.0 Hz, 2 H), 1.90 - 2.19 (m, 8 H)

Cpd Number	^{1}H NMR data
629	(400 MHz, $CDCl_3$) δ ppm 7.90 - 8.08 (m, 2 H), 7.45 (s, 1 H), 7.13 - 7.36 (m, 2 H), 5.65 (d, *J*=4.6 Hz, 1 H), 3.87 - 4.00 (m, 1 H), 3.82 (d, *J*=12.2 Hz, 2 H), 3.65 (br. s., 1 H), 3.39 (s, 3 H), 3.15 - 3.45 (m, 4 H), 3.04 (t, *J*=12.0 Hz, 2 H), 2.73 - 2.87 (m, 3 H), 2.35 - 2.70 (m, 9 H), 1.94 - 2.22 (m, 6 H)
630	(400 MHz, DMSO-d_6) δ ppm 8.28 - 8.43 (m, 2 H), 7.40 (d, *J*=8.9 Hz, 2 H), 7.35 (br. s., 2 H), 7.26 (s, 1 H), 3.98 (quin, *J*=8.2 Hz, 1 H), 3.66 (d, *J*=12.1 Hz, 2 H), 3.35 (br. s., 2 H), 3.26 (s, 3 H), 3.01 - 3.18 (m, 3 H), 2.96 (t, *J*=11.9 Hz, 2 H), 2.82 (br. s., 2 H), 2.36 - 2.47 (m, 3 H), 2.05 - 2.22 (m, 3 H), 1.93 - 2.04 (m, 3 H), 1.77 - 1.92 (m, 2 H), 1.67 (br. s., 2 H)
631	HCl salt (300 MHz, $CDCl_3$) δ ppm 10.10 (br. s., 1 H), 9.95 (br. s., 1 H), 7.78 (s, 1 H), 7.45 - 7.68 (m, 3 H), 4.87 - 5.06 (m, 1 H), 4.53 - 4.82 (m, 1 H), 3.50 - 3.97 (m, 8 H), 3.33 - 3.45 (m, 3 H), 3.15 (br. s., 2 H), 1.92 (d, *J*=13.2 Hz, 5 H), 1.73 (d, *J*=10.3 Hz, 1 H), 1.51 (d, *J*=11.0 Hz, 2 H), 1.02 - 1.33 (m, 10 H)
632	(300 MHz, $CDCl_3$) δ ppm 7.75 - 7.97 (m, 2 H), 7.02 - 7.24 (m, 3 H), 4.14 (t, *J*=7.8 Hz, 4 H), 3.63 - 3.89 (m, 3 H), 3.55 (br. s., 1 H), 3.18 - 3.28 (m, 6 H), 3.10 (br. s., 2 H), 2.91 (t, *J*=12.3 Hz, 2 H), 2.27 - 2.59 (m, 8 H), 2.17 (quin, *J*=7.7 Hz, 3 H), 1.82 - 2.07 (m, 5 H)

Cpd Number	^{1}H NMR data
633	(300 MHz, $CDCl_3$) δ ppm 7.88 (s, 1 H), 7.74 (d, *J*=8.1 Hz, 2 H), 7.62 (d, *J*=7.7 Hz, 2 H), 5.05 (dt, *J*=12.2, 6.2 Hz, 1 H), 4.70 - 4.87 (m, 1 H), 4.19 - 4.35 (m, 2 H), 4.09 (br. s., 2 H), 3.82 (br. s., 2 H), 3.64 (br. s., 1 H), 3.41 - 3.52 (m, 3 H), 2.40 (br. s., 6 H), 1.87 - 2.11 (m, 6 H), 1.79 (d, *J*=13.6 Hz, 1 H), 1.58 (d, *J*=12.5 Hz, 3 H), 1.27 - 1.37 (m, 6 H)
634	(400 MHz, $CDCl_3$) δ ppm 7.84 - 7.93 (m, 1 H), 7.67 (d, *J*=8.1 Hz, 2 H), 7.40 (d, *J*=8.1 Hz, 2 H), 5.01 (dt, *J*=12.2, 6.1 Hz, 1 H), 4.72 - 4.87 (m, 1 H), 3.59 (s, 2 H), 3.38 - 3.46 (m, 3 H), 2.50 - 2.94 (m, 8 H), 1.85 - 2.15 (m, 9 H), 1.77 (d, *J*=12.2 Hz, 1 H), 1.48 - 1.63 (m, 2 H), 1.30 (d, *J*=6.1 Hz, 6 H), 1.14 (d, *J*=6.1 Hz, 6 H)
635	(300 MHz, $CDCl_3$) δ ppm 10.10 (br. s., 1 H), 7.82 (s, 1 H), 7.60 - 7.77 (m, 4 H), 4.98 (dt, *J*=12.4, 6.1 Hz, 1 H), 4.73 (d, *J*=5.5 Hz, 1 H), 4.12 (d, *J*=4.0 Hz, 2 H), 3.54 (br. s., 1 H), 3.40 (s, 3 H), 3.11 - 3.32 (m, 5 H), 2.83 - 3.04 (m, 2 H), 2.43 (t, *J*=13.2 Hz, 2 H), 1.81 - 2.06 (m, 8 H), 1.73 (d, *J*=12.8 Hz, 2 H), 1.38 - 1.60 (m, 2 H), 1.15 - 1.29 (m, 6 H)
636	(300 MHz, $CDCl_3$) δ ppm 7.90 (s, 1 H), 7.69 (d, *J*=8.1 Hz, 2 H), 7.44 (d, *J*=8.1 Hz, 2 H), 5.04 (dt, *J*=12.2, 6.2 Hz, 1 H), 4.72 - 4.86 (m, 1 H), 3.72 - 3.82 (m, 2 H), 3.51 - 3.71 (m, 3 H), 3.45 (s, 3 H), 3.10 - 3.23 (m, 2 H), 2.72 - 2.90 (m, 6 H), 2.48 (br. s., 2 H), 1.88 - 2.10 (m, 6 H), 1.69 - 1.86 (m, 1 H), 1.42 - 1.66 (m, 3 H), 1.31 (d, *J*=5.9 Hz, 6 H)

Cpd Number	^{1}H NMR data
637	(400 MHz, $CDCl_3$) δ ppm 7.91 (s, 1 H), 7.77 (d, *J*=8.1 Hz, 2 H), 7.62 (d, *J*=8.3 Hz, 2 H), 5.07 (dt, *J*=12.2, 6.1 Hz, 1 H), 4.74 - 4.86 (m, 1 H), 3.52 - 3.96 (m, 3 H), 3.47 (s, 3 H), 3.23 (s, 2 H), 3.05 - 3.18 (m, 3 H), 2.71 - 2.86 (m, 1 H), 2.71 - 2.86 (m, 1 H), 2.61 (s, 3 H), 1.89 - 2.09 (m, 6 H), 1.80 (d, *J*=12.7 Hz, 1 H), 1.51 - 1.69 (m, 3 H), 1.32 (d, *J*=6.1 Hz, 6 H)
638	(400 MHz, $CDCl_3$) δ ppm 7.91 - 8.01 (m, 2 H), 7.39 (s, 1 H), 7.17 - 7.26 (m, 2 H), 3.85 - 3.97 (m, 1 H), 3.67 (t, *J*=6.0 Hz, 2 H), 3.42 (br. s., 2 H), 3.10 (br. s., 3 H), 2.85 - 2.97 (m, 3 H), 2.74 (br. s., 3 H), 2.71 (s, 3 H), 2.48 - 2.63 (m, 3 H), 2.38 (dtd, *J*=12.0, 8.1, 8.1, 3.7 Hz, 2 H), 1.94 - 2.13 (m, 4 H), 1.74 (d, *J*=8.1 Hz, 2 H), 1.41 (d, *J*=5.9 Hz, 6 H)
639	(300 MHz, $CDCl_3$) δ ppm 7.91 (s, 1 H), 7.76 - 7.85 (m, 2 H), 7.66 (d, *J*=8.4 Hz, 2 H), 5.07 (quin, *J*=6.1 Hz, 1 H), 4.67 - 4.90 (m, 1 H), 3.48 (s, 3 H), 3.28 (br. s., 2 H), 2.85 (br. s., 2 H), 2.62 (br. s., 5 H), 2.25 (d, *J*=13.6 Hz, 2 H), 1.87 - 2.11 (m, 6 H), 1.81 (d, *J*=12.8 Hz, 1 H), 1.39 - 1.69 (m, 3 H), 1.33 (d, *J*=6.2 Hz, 6 H)
640	(400 MHz, $CDCl_3$) δ ppm 7.92 (s, 1 H), 7.69 - 7.81 (m, 4 H), 5.07 (dt, *J*=12.2, 6.1 Hz, 1 H), 4.80 (br. s., 1 H), 4.36 (br. s., 3 H), 4.23 (br. s., 1 H), 3.47 (s, 3 H), 3.35 (br. s., 1 H), 2.36 (br. s., 6 H), 1.90 - 2.10 (m, 6 H), 1.81 (d, *J*=11.7 Hz, 1 H), 1.59 (d, *J*=12.5 Hz, 2 H), 1.24 - 1.41 (m, 7 H)
641	(300 MHz, $CDCl_3$) δ ppm 7.92 (s, 1 H), 7.72 (d, *J*=8.1 Hz, 2 H), 7.47 (d, *J*=8.1 Hz, 2 H), 5.06 (dt, *J*=12.2, 6.2 Hz, 1 H), 4.92 (br. s., 2 H), 4.79 (br. s., 1 H), 3.47 (s, 3 H), 2.71 (br. s., 6 H), 1.89 - 2.09 (m, 6 H), 1.44 - 1.86 (m, 8 H), 1.28 - 1.42 (m, 9 H)

Cpd Number	^{1}H NMR data
643	(400 MHz, $CDCl_3$) δ ppm 7.92 (s, 1 H), 7.70 (d, *J*=8.1 Hz, 2 H), 7.43 (d, *J*=7.1 Hz, 2 H), 4.99 - 5.10 (m, 1 H), 4.79 (br. s., 1 H), 3.64 (br. s., 2 H), 3.47 (s, 3 H), 3.12 (d, *J*=11.0 Hz, 3 H), 2.75 (s, 6 H), 2.19 (d, *J*=10.0 Hz, 4 H), 1.93 - 2.08 (m, 8 H), 1.76 - 1.92 (m, 2 H), 1.51 - 1.66 (m, 2 H), 1.33 (d, *J*=6.1 Hz, 6 H)
645	(400 MHz, $CDCl_3$) δ ppm 8.17 (d, *J*=6.6 Hz, 2 H), 8.02 (dd, *J*=7.8, 4.9 Hz, 2 H), 6.65 (d, *J*=6.8 Hz, 2 H), 4.33 (br. s., 2 H), 4.19 (br. s., 3 H), 3.96 (t, *J*=7.8 Hz, 1 H), 3.78 (d, *J*=12.2 Hz, 2 H), 3.38 (s, 3 H), 3.27 (s, 3 H), 3.08 (d, *J*=9.3 Hz, 2 H), 3.00 (t, *J*=11.9 Hz, 2 H), 2.90 (br. s., 2 H), 2.54 - 2.69 (m, 2 H), 2.45 (d, *J*=8.3 Hz, 2 H), 2.30 (br. s., 4 H), 1.82 - 2.19 (m, 7 H)
647	(400 MHz, DMSO-d_6) δ ppm 8.42 - 8.52 (m, 2 H), 7.33 - 7.43 (m, 2 H), 7.29 (s, 1 H), 3.96 (quin, *J*=8.3 Hz, 1 H), 3.55 - 3.69 (m, 6 H), 3.40 (br. s., 3 H), 3.26 (s, 3 H), 3.20 (br. s., 3 H), 3.09 - 3.16 (m, 4 H), 2.98 (br. s., 2 H), 2.88 (t, *J*=11.9 Hz, 2 H), 2.34 - 2.45 (m, 2 H), 1.92 - 2.21 (m, 6 H), 1.77 - 1.91 (m, 2 H), 1.70 (br. s., 2 H)
648	(400 MHz, $CDCl_3$) δ ppm 8.05 (s, 1 H), 8.01 (d, *J*=7.9 Hz, 2 H), 7.57 (t, *J*=7.7 Hz, 2 H), 7.33 - 7.44 (m, 1 H), 4.02 (quin, *J*=8.3 Hz, 1 H), 3.81 (t, *J*=4.6 Hz, 4 H), 3.29 - 3.32 (m, 4 H), 2.60 - 2.77 (m, 2 H), 2.43 - 2.58 (m, 6 H), 2.33 (br. s., 1 H), 2.14 - 2.25 (m, 3 H), 1.99 - 2.13 (m, 3 H), 1.52 - 1.67 (m, 4 H)

Cpd Number	^{1}H NMR data
649	(400 MHz, $CDCl_3$) δ ppm 8.09 (d, *J*=7.7 Hz, 2 H), 8.02 (s, 1 H), 7.55 (t, *J*=7.5 Hz, 2 H), 7.35 (t, *J*=7.1 Hz, 1 H), 4.01 (quin, *J*=8.3 Hz, 1 H), 3.80 (t, *J*=4.6 Hz, 4 H), 3.25 - 3.37 (m, 1 H), 3.03 (s, 6 H), 2.59 - 2.74 (m, 2 H), 2.42 - 2.58 (m, 6 H), 2.33 (br. s., 1 H), 2.14 - 2.25 (m, 3 H), 1.97 - 2.13 (m, 3 H), 1.53 - 1.68 (m, 4 H)
650	(400 MHz, $CDCl_3$) δ ppm 7.86 - 8.08 (m, 2 H), 7.14 - 7.36 (m, 3 H), 4.75 - 4.87 (m, 0.5 H), 4.68 (t, *J*=4.9 Hz, 0.5 H), 4.00 (quin, *J*=8.4 Hz, 2 H), 3.72 (d, *J*=12.5 Hz, 2 H), 2.88 - 3.02 (m, 2 H), 2.78 - 2.86 (m, 2 H), 2.76 (s, 3 H), 2.57 - 2.67 (m, 4 H), 2.48 - 2.55 (m, 1 H), 2.33 - 2.47 (m, 2 H), 1.69 - 2.19 (m, 10 H)
651	(300 MHz, TFA) δ ppm 7.53 (s, 1 H), 7.45 - 7.52 (m, 2 H), 7.24 (t, *J*=8.4 Hz, 2 H), 4.44 (d, *J*=13.3 Hz, 2 H), 4.23 (t, *J*=7.8 Hz, 4 H), 4.11 (d, *J*=12.9 Hz, 2 H), 3.90 - 4.05 (m, 3 H), 3.58 - 3.88 (m, 8 H), 2.36 - 2.55 (m, 6 H), 2.28 (quin, *J*=7.8 Hz, 2 H), 2.05 - 2.21 (m, 3 H), 1.91 - 2.04 (m, 1 H), 1.39 (d, *J*=6.6 Hz, 6 H)
652	(400 MHz, DMSO-d_6) δ ppm 8.15 – 8.07 (m, 2H), 7.57 (t, 1H), 7.30 (s, 1H), 7.12 (t, 1H), 7.10 (s, 1H), 4.05 – 3.93 (m, 1H), 3.67 – 3.60 (m, 6H), 3.05 – 2.97 (m, buried), 2.90 (s, 6H), 2.63 (s, from $Me_2NSO_2NH_2$ impurity), 2.61 – 2.55 (m, 4H), 2.47 – 2.42 (m, buried), 2.12 – 1.92 (m, 4H), 1.75 – 1.62 (m, 2H)
656	(400 MHz, 120 °C, DMSO-d_6) δ ppm 8.11 (d, *J* = 8.0 Hz, 2H), 7.52 (t, *J* = 7.8 Hz, 2H), 7.31 (t, *J* = 7.5 Hz, 1H), 6.91 (s, 1H), 4.02 (p, *J* = 8.3 Hz, 1H), 3.65 – 3.58 (m, 6H), 3.36 (s, 3H), 3.30 (s, 3H), 3.01 (t, 2H), 2.56 (t, *J* = 4.7 Hz, 4H), 2.53 – 2.38 (m, 4H), 2.12 – 1.93 (m, 5H), 1.77 – 1.65 (m, 2H)

Cpd Number	^{1}H NMR data
657	(400 MHz, $CDCl_3$) δ ppm 8.11 – 8.05 (m, 2H), 7.48 (dd, *J* = 8.5, 7.4 Hz, 2H), 7.33 – 7.27 (m, 1H), 6.93 (s, 1H), 4.04 – 3.93 (m, 1H), 3.69 – 3.60 (m, 2H), 3.42 (s, 3H), 3.40 (s, 3H), 3.37 (d, *J* = 6.3 Hz, 2H), 3.26 (s, 3H), 2.90 (td, *J* = 12.4, 2.4 Hz, 2H), 2.63 (dq, *J* = 11.7, 9.2 Hz, 2H), 2.48 – 2.36 (m, 2H), 2.14 – 2.02 (m, 2H), 1.94 (dd, *J* = 13.5, 3.1 Hz, 2H), 1.91 – 1.80 (m, 1H), 1.63 – 1.50 (m, 2H)
658	(400 MHz, pyridine-d_5) δ ppm 8.43 – 8.31 (m, 2H), 7.49 (m, 2H), 7.37 (s, 1H), 7.31 (t, *J* = 7.5 Hz, 1H), 3.88 – 3.72 (m, 6H), 3.54 (s, 5H), 3.01 – 2.78 (m, 2H), 2.77 – 2.67 (m, 2H), 2.61 – 2.49 (m, 7H), 2.38 (d, *J* = 14.7 Hz, 1H), 2.44 – 2.30 (m, 1H), 2.16 – 2.04 (m, 2H), 1.97 (d, *J* = 13.1 Hz, 2H), 1.86 – 1.74 (m, 2H), 1.28 (t, *J* = 7.4 Hz, 3H)
659	(400 MHz, pyridine-d_5) δ ppm 8.33 (dd, *J* = 7.6, 1.3 Hz, 2H), 7.50 – 7.44 (m, 2H), 7.32 – 7.23 (m, 1H), 7.06 (s, 1H), 3.97 (q, *J* = 8.3 Hz, 1H), 3.90 (q, *J* = 7.4 Hz, 2H), 3.53 (s, 3H), 3.42 (d, *J* = 12.4 Hz, 2H), 3.27 (d, *J* = 66.7 Hz, 3H), 2.94 (d, *J* = 6.6 Hz, 2H), 2.79 – 2.63 (m, 4H), 2.53 – 2.43 (m, 1H), 2.20 – 1.94 (m, 5H), 1.85 (d, *J* = 3.5 Hz, 2H), 1.70 – 1.49 (m, 2H), 1.20 (t, *J* = 7.4 Hz, 3H)
660	(400 MHz, pyridine-d_5) δ ppm 8.74 – 8.67 (m, 2H), 7.53 (d, *J* = 8.8 Hz, 2H), 7.29 – 7.19 (m, 1H), 7.09 (s, 1H), 4.33 – 4.25 (m, 2H), 3.96 (s, 1H), 3.64 – 3.52 (m, 2H), 3.41 (d, *J* = 12.4 Hz, 2H), 3.20 (s, 1H), 2.95 (d, *J* = 6.6 Hz, 2H), 2.83 (s, 3H), 2.65 (td, *J* = 10.0, 9.3, 2.2 Hz, 4H), 2.46 – 2.33 (m, 2H), 2.01 (dd, *J* = 12.1, 8.4 Hz, 4H), 1.88 – 1.70 (m, 6H), 1.55 (qd, *J* = 12.2, 3.7 Hz, 2H)

Cpd Number	^{1}H NMR data
661	(400 MHz, pyridine-d_5) δ ppm 8.79 (d, J = 8.0 Hz, 2H), 7.61 – 7.54 (m, 2H), 7.26 (t, 1H), 7.18 (s, 1H), 4.16 (t, J = 6.8 Hz, 2H), 3.96 (t, J = 8.3 Hz, 1H), 3.51 (t, J = 7.1 Hz, 2H), 3.39 (d, J = 12.3 Hz, 2H), 3.12 (s, 3H), 2.89 (d, J = 6.7 Hz, 2H), 2.71 – 2.59 (m, 4H), 2.45 – 2.28 (m, 4H), 2.08 – 1.94 (m, 4H), 1.86 – 1.78 (m, 4H), 1.61 – 1.47 (m, 2H)
662	(400 MHz, pyridine-d_5) δ ppm 8.40 – 8.32 (m, 2H), 7.49 – 7.41 (m, 2H), 7.32 – 7.21 (m, 1H), 7.06 (s, 1H), 4.02 – 3.90 (m, 1H), 3.64 (s, 3H), 3.53 (s, 3H), 3.42 (d, J = 12.4 Hz, 2H), 3.19 (s, 1H), 2.94 (d, J = 6.8 Hz, 2H), 2.74 – 2.60 (m, 4H), 2.41 (qt, J = 8.3, 4.1 Hz, 2H), 2.10 – 1.97 (m, 4H), 1.88 – 1.77 (m, 4H), 1.63 – 1.49 (m, 2H)
663	(400 MHz, pyridine-d_5) δ ppm 8.68 (t, 2H), 7.52 (d, J = 6.4 Hz, 2H), 7.22 (tt, J = 7.5, 1.2 Hz, 1H), 7.03 (s, 1H), 4.24 (s, 2H), 4.02 – 3.89 (m, 1H), 3.50 – 3.42 (m, 2H), 3.38 (d, J = 12.4 Hz, 2H), 3.17 (s, 1H), 2.92 (d, J = 6.6 Hz, 2H), 2.62 (qd, J = 9.1, 4.3 Hz, 4H), 2.39 (qt, J = 8.1, 3.8 Hz, 2H), 2.13 – 1.94 (m, 6H), 1.87 – 1.77 (m, 4H), 1.68 (td, J = 7.1, 6.3, 4.3 Hz, 2H), 1.61 – 1.47 (m, 2H)
664	(400 MHz, pyridine-d_5) δ ppm 8.66 (m, 2H), 7.52 – 7.46 (m, 2H), 7.25 (t, J = 7.4 Hz, 1H), 4.11 (t, J = 8.1 Hz, 1H), 3.79 – 3.72 (m, 5H), 3.62 – 3.53 (m, 4H), 2.87 (s, 4H), 2.8 (m, 2H), 2.71 (dq, J = 11.4, 8.9 Hz, 2H), 2.61 – 2.45 (m, 7H), 2.41 – 2.30 (m, 1H), 2.14 – 2.03 (m, 2H), 1.96 (d, J = 12.7 Hz, 2H), 1.89 – 1.75 (m, 4H)

Cpd Number	^{1}H NMR data
665	(400 MHz, pyridine-d_5) δ ppm 8.43 – 8.31 (m, 2H), 7.49 (m, 2H), 7.37 (s, 1H), 4.25 – 4.15 (m, 2H), 3.80 – 3.70 (m, 4H), 3.57 (d, J = 12.6 Hz, 2H), 3.48 – 3.36 (m, 2H), 2.85 (td, J = 12.1, 2.5 Hz, 2H), 2.71 (dq, J = 11.6, 8.7 Hz, 2H), 2.63 – 2.44 (m, 6H), 2.35 (p, J = 7.2 Hz, 2H), 2.15 – 2.02 (m, 2H), 1.95 (d, J = 12.6 Hz, 2H), 1.88 – 1.65 (m, 2H)
666	(400 MHz, pyridine-d_5) δ ppm 8.43 – 8.31 (m, 2H), 7.49 (m, 2H), 7.37 (s, 1H), 4.31 – 4.22 (m, 2H), 3.75 – 3.69 (m, 4H), 3.56 (d, J = 12.7 Hz, 2H), 3.43 – 3.32 (m, 2H), 2.90 – 2.77 (m, 2H), 2.72 (dd, J = 20.0, 8.8 Hz, 2H), 2.60 – 2.52 (m, 4H), 2.50 (dt, J = 8.1, 4.2 Hz, 2H), 2.41 – 2.27 (m, 1H), 2.22 – 2.03 (m, 4H), 1.97 – 1.89 (m, 2H), 1.84 – 1.70 (m, 4H)
667	(400 MHz, pyridine-d_5) δ ppm 8.75 – 8.67 (m, 2H), 7.59 – 7.52 (m, 2H), 7.31 – 7.22 (m, 2H), 4.16 (t, J = 6.8 Hz, 2H), 4.09 – 4.00 (m, 1H), 3.56 – 3.46 (m, 2H), 3.41 – 3.37 (m, 2H), 3.30 (s, 3H), 3.28 (d, J = 5.8 Hz, 2H), 2.79 (td, J = 12.2, 2.3 Hz, 2H), 2.69 – 2.61 (m, 2H), 2.46 (ddd, J = 9.5, 4.3, 2.6 Hz, 2H), 2.37 – 2.28 (m, 2H), 2.14 – 1.97 (m, 2H), 1.89 – 1.66 (m, 3H), 1.57 (td, J = 12.2, 4.0 Hz, 2H)
668	(400 MHz, pyridine-d_5) δ ppm 8.64 – 8.59 (m, 2H), 7.53 – 7.47 (m, 2H), 7.28 – 7.21 (m, 1H), 7.11 (d, J = 0.7 Hz, 1H), 4.31 – 4.23 (m, 2H), 4.08 (p, J = 8.2 Hz, 1H), 3.50 (s, 2H), 3.38 (s, 2H), 3.32 (s, J = 0.6 Hz, 3H), 3.30 (d, J = 5.8 Hz, 2H), 2.80 (td, J = 12.1, 2.4 Hz, 2H), 2.69 (pd, J = 8.8, 2.5 Hz, 2H), 2.47 (dddd, J = 12.1, 10.2, 7.6, 4.3 Hz, 2H), 2.20 – 1.96 (m, 4H), 1.85 (d, J = 11.9 Hz, 2H), 1.82 – 1.69 (m, 3H), 1.65 – 1.51 (m, 2H)

Cpd Number	^{1}H NMR data
669	^{1} NMR (400 MHz, $CDCl_3$) δ ppm 9.96 (br. s., 1 H), 7.96 - 8.05 (m, 2 H), 7.44 (s, 1 H), 7.21 - 7.30 (m, 2 H), 5.24 - 5.26 (m, 1 H), 3.98 (t, *J*=8.4 Hz, 1 H), 3.69 (d, *J*=12.5 Hz, 2 H), 3.33 - 3.45 (m, 5 H), 2.89 - 3.02 (m, 2 H), 2.78 (d, *J*=5.4 Hz, 2 H), 2.55 - 2.69 (m, 2 H), 2.36 - 2.49 (m, 2 H), 2.03 - 2.16 (m, 3 H), 1.87 - 1.99 (m, 3 H), 1.51 - 1.66 (m, 2H)
670	^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.96 (br. s., 1 H), 7.97 - 8.09 (m, 2 H), 7.45 (s, 1 H), 7.15 - 7.32 (m, 2 H), 3.94 - 4.04 (m, 1 H), 3.83 - 3.90 (m, 2 H), 3.75 - 3.82 (m, 2 H), 3.69 (d, *J*=12.5 Hz, 2 H), 3.35 - 3.44 (m, 5 H), 3.26 (s, 3 H), 2.87 - 3.05 (m, 2 H), 2.54 - 2.70 (m, 2 H), 2.37 - 2.50 (m, 2 H), 2.03 - 2.14 (m, 2 H), 1.91 - 2.00 (m, 3 H), 1.55 - 1.69 (m, 2 H)
671	^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.97 (br. s., 1 H), 7.93 - 8.06 (m, 2 H), 7.45 (s, 1 H), 7.15 - 7.28 (m, 2 H), 3.98 (t, *J*=8.3 Hz, 1 H), 3.74 - 3.83 (m, 4 H), 3.69 (d, *J*=12.5 Hz, 2 H), 3.47 - 3.55 (m, 4 H), 3.34 - 3.43 (m, 5 H), 2.88 - 3.04 (m, 2 H), 2.55 - 2.66 (m, 2 H), 2.44 (dq, *J*=7.9, 4.0 Hz, 2 H), 2.03 - 2.20 (m, 2 H), 1.86 - 2.01 (m, 3 H), 1.52 - 1.68 (m, 2 H)
672	^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.93 (br. s., 1 H), 7.99 (dd, *J*=8.3, 4.6 Hz, 2 H), 7.45 (s, 1 H), 7.22 - 7.32 (m, 2 H), 3.98 (quin, *J*=8.2 Hz, 1 H), 3.82 (t, *J*=5.6 Hz, 1 H), 3.65 - 3.75 (m, 2 H), 3.35 - 3.44 (m, 5 H), 2.96 (t, *J*=11.9 Hz, 2 H), 2.56 - 2.66 (m, 2 H), 2.43 (d, *J*=7.8 Hz, 2 H), 2.12 - 2.20 (m, 2 H), 2.08 (dd, *J*=17.6, 8.6 Hz, 2 H), 2.01 - 2.12 (m, 2 H), 1.88 - 1.99 (m, 3 H), 1.58 (d, *J*=11.5 Hz, 4 H)

Cpd Number	^{1}H NMR data
673	^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 10.08 (br. s., 1 H), 7.95 - 8.07 (m, 2 H), 7.44 (s, 1 H), 7.18 - 7.34 (m, 2 H), 5.36 (d, *J*=6.8 Hz, 1 H), 4.10 (q, *J*=7.1 Hz, 2 H), 3.94 - 4.04 (m, 3 H), 3.70 (d, *J*=12.2 Hz, 2 H), 3.46 - 3.58 (m, 1 H), 3.33 - 3.43 (m, 5 H), 2.87 - 3.05 (m, 4 H), 2.55 - 2.68 (m, 2 H), 2.38 - 2.48 (m, 2 H), 2.03 - 2.16 (m, 2 H), 1.87 - 2.00 (m, 5 H), 1.41 - 1.62 (m, 4 H), 1.24 (t, *J*=7.2 Hz, 3 H)
674	^{1} NMR (400 MHz, $CDCl_3$) δ ppm 9.96 (br. s., 1 H), 7.96 - 8.05 (m, 2 H), 7.44 (s, 1 H), 7.21 - 7.30 (m, 2 H), 6.01 – 6.05 (m, 1 H), 4.82 (t, *J*=6.9 Hz, 2 H), 4.65 – 4.75 (m, 1 H), 4.59 (t, *J*=6.7 Hz, 2 H), 3.92 – 4.01 (m, 1 H), 3.64 - 3.72 (m, 2 H), 3.40 (s, 3 H), 3.35 - 3.38 (m, 2 H), 2.90 - 3.00 (m, 2 H), 2.54 – 2.66 (m, 2 H), 2.36 – 2.47 (m, 2 H), 1.84 - 2.16 (m, 5 H), 1.48 - 1.64 (m, 2H).
675	^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 10.05 (br. s., 1 H), 7.96 - 8.03 (m, 2 H), 7.43 (s, 1 H), 7.21 – 7.29 (m, 2 H), 5.29 – 5.36 (m, 1 H), 3.85 - 4.02 (m, 3 H), 3.64 - 3.72 (m, 2 H), 3.51 - 3.61 (m, 1 H), 3.33 - 3.44 (m, 7 H), 2.92 - 3.00 (m, 2 H), 2.55 - 2.65 (m, 2 H), 2.36 - 2.47 (m, 2 H), 1.84 - 2.15 (m, 7 H), 1.49 – 1.67 (m, 4 H).
676	^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 9.94 (br. s., 1 H), 7.92 - 8.07 (m, 2 H), 7.44 (s, 1 H), 7.18 - 7.31 (m, 2 H), 3.92 - 4.06 (m, 3 H), 3.64 - 3.76 (m, 6 H), 3.33 - 3.44 (m, 7 H), 2.88 - 3.10 (m, 4 H), 1.20 - 2.71 (m, 18 H)

Cpd Number	^{1}H NMR data
677	^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.96 (br. s., 1 H), 7.94 - 8.04 (m, 2 H), 7.47 (s, 1 H), 7.22 - 7.30 (m, 2 H), 4.21 (q, *J*=7.1 Hz, 2 H), 4.04 – 3.92 (m, 1 H), 3.90 – 3.85 (m, 2 H), 3.74 - 3.82 (m, 6 H), 3.22 - 3.22 (m, 7 H), 2.57 - 2.68 (m, 2 H), 2.38 - 2.48 (m, 2 H), 2.02 - 2.15 (m, 2H), 1.32 (t, *J*=6.7 Hz, 3 H).
678	^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.96 (br. s., 1 H), 7.94 - 8.01 (m, 2 H), 7.47 (s, 1 H), 7.22 - 7.30 (m, 2 H), 4.21 (q, *J*=7.1 Hz, 2 H), 4.04 – 3.92 (m, 1 H), 3.72 - 3.82 (m, 8 H), 3.46 - 3.52 (m, 4 H), 3.24 - 3.32 (m, 4 H), 2.57 - 2.68 (m, 2 H), 2.38 - 2.48 (m, 2 H), 2.02 - 2.15 (m, 2H), 1.31 (t, *J*=6.7 Hz, 3 H).
679	^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.96 (br. s., 1 H), 7.94 - 8.01 (m, 2 H), 7.48 (s, 1 H), 7.22 - 7.30 (m, 2 H), 4.21 (q, *J*=7.1 Hz, 2 H), 4.04 – 3.92 (m, 1 H), 3.76 - 3.82 (m, 4 H), 3.41 (s, 3 H), 3.24 - 3.31 (m, 4 H), 2.57 - 2.68 (m, 2 H), 2.38 - 2.48 (m, 2 H), 2.02 - 2.15 (m, 2H), 1.31 (t, *J*=6.7 Hz, 3 H).
680	^{1}H NMR (300 MHz, $CDCl_3$) □ ppm 7.91 - 8.09 (m, 2 H), 7.46 (s, 1 H), 7.22 - 7.34 (m, 2 H), 5.38 (d, *J*=5.0 Hz, 1 H), 4.22 (q, *J*=7.2 Hz, 2 H), 3.99 (quin, *J*=8.3 Hz, 1 H), 3.75 - 3.85 (m, 4 H), 3.24 - 3.32 (m, 4 H), 2.79 (d, *J*=4.0 Hz, 3 H), 2.56 - 2.68 (m, 2 H), 2.36 - 2.49 (m, 2 H), 2.01 - 2.14 (m, 2 H), 1.24 - 1.36 (t, *J*=7.2 Hz, 3 H)
681	^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.96 - 8.02 (m, 2 H), 7.49 (s, 1 H), 7.22 - 7.27 (m, 2 H), 4.04 – 3.92 (m, 3 H), 3.75 - 3.82 (m, 4 H), 3.28 - 3.34 (m, 4 H), 2.57 - 2.68 (m, 2 H), 2.38 - 2.48 (m, 2 H), 1.94 - 2.15 (m, 3 H), 0.97 (d, *J*=6.7 Hz, 6 H).

Cpd Number	^{1}H NMR data
682	^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.72 (br. s., 1 H), 7.72 - 7.89 (m, 2 H), 7.27 (s, 1 H), 6.98 - 7.12 (m, 2 H), 3.67 - 3.86 (m, 3 H), 3.52 - 3.63 (m, 8 H), 3.22 - 3.35 (m, 4 H), 3.09 (br. s., 4 H), 2.36 - 2.50 (m, 2 H), 2.23 (dd, *J*=7.7, 4.3 Hz, 2 H), 1.72 - 1.99 (m, 3 H), 0.78 (d, *J*=6.6 Hz, 6 H)
683	^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.92 (s, 1 H), 7.91 - 8.07 (m, 2 H), 7.48 (s, 1 H), 7.22 - 7.34 (m, 2 H), 4.80 (br. s., 2 H), 3.74 - 4.02 (m, 8 H), 3.59 - 3.69 (m, 1 H), 3.34 - 3.46 (m, 6 H), 3.22 - 3.32 (m, 4 H), 2.54 - 2.72 (m, 1 H), 2.35 - 2.46 (m, 1 H), 1.88 - 2.18 (m, 2 H), 0.98 (d, *J*=6.8 Hz, 6 H)
684	^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.92 (br. s., 1 H), 7.93 - 8.07 (m, 2 H), 7.47 (s, 1 H), 7.19 - 7.32 (m, 2 H), 5.25 - 5.35 (m, 1 H), 3.92 - 4.06 (m, 3 H), 3.72 - 3.85 (m, 2 H), 3.18 - 3.36 (m, 2 H), 2.79 (d, *J*=5.4 Hz, 2 H), 2.56 - 2.72 (m, 2 H), 2.34 - 2.52 (m, 2H), 1.89 - 2.19 (m, 4 H), 1.59 (br. s., 4 H), 0.99 (d, *J*=6.6 Hz, 6 H)
686	^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 10.30 (br. s., 1 H), 8.17 - 8.34 (m, 2 H), 8.01 (dd, *J*=8.7, 4.8 Hz, 2 H), 7.35 (s, 1 H), 7.20 - 7.31 (m, 2 H), 6.78 (dd, *J*=7.7, 4.8 Hz, 1 H), 5.94 (br. s., 2 H), 3.95 (quin, *J*=8.3 Hz, 1 H), 3.64 (d, *J*=12.2 Hz, 2 H), 3.29 - 3.42 (m, 5 H), 2.91 (t, *J*=12.0 Hz, 2 H), 2.53 - 2.67 (m, 2 H), 2.42 (d, *J*=8.3 Hz, 2 H), 2.02 - 2.13 (m, 2 H), 1.83 - 1.97 (m, 2 H), 1.49 - 1.69 (m, 3 H)

Determination of Biological Activity

Cellular Assays

Measuring CFTR cell surface expression of CFTR- ΔF508 using PathHunter® U2OS CFTR-ΔF508 cells

[00795] The PathHunter® U2OS CFTR-ΔF508 cell assay (DiscoveRx) measures the expression of CFTR-ΔF508 at the plasma membrane. CFTR-ΔF508 has a folding defect leading to absence of protein at the plasma membrane. This assay is used to evaluate the capacity of compounds to increase the expression of CFTR-ΔF508 at the plasma membrane. The CFTR-ΔF508 is tagged with a ProLink™ peptide which can complement with plasma membrane expressed enzyme acceptor protein (EA-MEM). When both the ProLink™ and EA-MEM acceptor are in close proximity, i.e. both are located at the plasma membrane; a functional enzyme is formed of which the activity can be measured. The amount of CFTR-ΔF508 that can be rescued to the plasma membrane is correlated with the amount of functional enzyme that can be measured.

[00796] There are several ways to measure the capacity of compounds to rescue CFTR-ΔF508 to the plasma membrane; either compounds are evaluated on their own and the impact on plasma membrane levels is measured or compounds are evaluated in combination with a co-corrector, i.e. a compound that rescues CFTR-ΔF508 to the plasma membrane but rescue can be enhanced by addition of compounds due to a complementary mode of action.

Activity of compounds in combination with co-corrector:

[00797] For this purpose, PathHunter® U2OS CFTR-ΔF508 cells (DiscoveRx; custom made were cultured in AssayComplete™ U2OS Cell Culture medium (DiscoveRx; 92-0018GK3) as per manufacturer's instructions. For compound testing, cells were seeded in white 384-well plates (Greiner; 781080) at five thousand cells/well in 25 µL AssayComplete™ Cell Plating 5 Reagent (DiscoveRx; 93-0563R5A) and incubated overnight at 37 °C, 5% CO_2. On day two, 5 µL of test compounds diluted in Cell Plating 5 Reagent were added to the cells with a final dimethyl sulfoxide (DMSO) concentration of 0.1%. In order to measure synergy with a co-corrector (3-[(2*R*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-7-methoxy-3,4-dihydro-2*H*-chromen-2-yl]benzoic acid), 3 µM of co-corrector was added along with test compounds. All cell plates contained 3 µM of co-corrector or DMSO as positive and negative controls, respectively. Cells were incubated with compounds for twenty to twenty-four hours at 37 °C, 5% CO_2. On day three, plates were placed at room temperature for thirty minutes and then 15 µL of substrate (PathHunter® Flash Detection Kit, DiscoveRx; 93-0247) was added

per well. After one hour of incubation at room temperature in the dark, the luminescence signal was measured on a plate reader (Envision®, Perkin Elmer). Raw data were normalized to percentage activity values using the equation: 100 × (Sample – Negative control)/(Positive control – Negative Control).

Activity of compounds for their intrinsic corrector capacity:

[00798] For this purpose PathHunter® U2OS CFTR-ΔF508 cells (DiscoveRx; custom made as described above) were cultured in AssayComplete™ U2OS Cell Culture medium (DiscoveRx; 92-0018GK3) as per manufacturer's instructions. For compound testing, cells were seeded in white 384-well plates (Greiner; 781080) at five thousand cells/well in 25 µL AssayComplete™ Cell Plating 5 Reagent (DiscoveRx; 93-0563R5A) and incubated overnight at 37 °C, 5% CO_2. On day two, 5 µL of test compounds diluted in Cell Plating 5 Reagent were added to the cells with a final DMSO concentration of 0.1%. All cell plates contained 3 µM corrector (3-[(2*R*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-7-methoxy-3,4-dihydro-2*H*-chromen-2-yl]benzoic acid) or DMSO as positive and negative controls, respectively. Cells were incubated with compounds for twenty to twenty-four hours at 37 °C, 5% CO_2. On day three, plates were placed at room temperature for thirty minutes and then 15 µL of substrate (PathHunter® Flash Detection Kit, DiscoveRx; 93-0247) was added per well. After one hour of incubation at room temperature in the dark, the luminescence signal was measured on a plate reader (Envision®, Perkin Elmer). Raw data were normalized to percentage activity values using the equation: 100 × (Sample – Negative control)/(Positive control – Negative Control).

Activity of compounds in presence of Human serum

[00799] To evaluate the impact of plasma protein binding of compounds on their biological activity, the PathHunter® U2OS CFTR-ΔF508 assay was run in the presence of 40% human serum (Sigma; H4522). For this purpose PathHunter® U2OS CFTR-ΔF508 cells (DiscoveRx; custom made) were cultured in AssayComplete™ U2OS Cell Culture medium (DiscoveRx; 92-0018GK3) as per manufacturer's instructions. For compound testing, cells were seeded in white 384-well plates (Greiner; 781080) at five thousand cells/well in 25 µL AssayComplete™ Cell Plating 5 Reagent (DiscoveRx; 93-0563R5A) containing 40% human serum and incubated overnight at 37 °C, 5% CO_2. On day two, 5 µL of test compounds diluted in Cell Plating 5 Reagent were added to the cells with a final DMSO concentration of 0.1%. All cell plates

contained 3μM corrector (4-[(2*R*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-7-methoxy-3,4-dihydro-2*H*-chromen-2-yl]benzoic acid) or DMSO as positive and negative controls respectively. Cells were incubated with compounds for twenty to twenty-four hours at 37 °C, 5% CO_2. On day three, plates were placed at room temperature for thirty minutes, and then 15 μL of substrate (PathHunter® Flash Detection Kit, DiscoveRx; 93-0247) was added per well. After one hour of incubation at room temperature in the dark, the luminescence signal was measured on a plate reader (Envision®, Perkin Elmer). Raw data were normalized to percentage activity values using the equation: 100 × (Sample – Negative control)/(Positive control – Negative Control).

Activity of compounds in presence of Human serum

[00800] To evaluate the impact of plasma protein binding of compounds on their biological activity, the PathHunter® U2OS CFTR-ΔF508 was run in the presence of 40% human serum (Sigma; H4522). For this purpose PathHunter® U2OS CFTR-ΔF508 cells (DiscoveRx; custom made) were cultured in AssayComplete™ U2OS Cell Culture medium (DiscoveRx; 92-0018GK3) as per manufacturer's instructions. For compound testing, cells were seeded in white 384-well plates (Greiner; 781080) at five thousand cells/well in 25 μL AssayComplete™ Cell Plating 5 Reagent (DiscoveRx; 93-0563R5A) and incubated overnight at 37 °C, 5% CO_2. On day two, the medium was replaced with 25 μL of primary human airway epithelial cell air-liquid interface medium or ALI medium, a 50:50 mixture of DMEM (Dulbecco's Modified Eagle Medium, Invitrogen; 41966-029) and LHC Basal Medium (Invitrogen; 12677-019) with additives as described in Table XVII) and containing 40% human serum. One hour later, 5 μL of test compounds diluted in ALI medium were added to the cells with a final DMSO concentration of 0.1%. All cell plates contained 3 μM corrector (4-[(2*R*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-7-methoxy-3,4-dihydro-2*H*-chromen-2-yl]benzoic acid) or DMSO as positive and negative controls respectively. Cells were incubated with compounds for twenty to twenty-four hours at 37 °C, 5% CO_2. On day three, plates were placed at room temperature for thirty minutes and then washed twice with PBS (phosphate buffered saline) followed by the addition of 15 μL of substrate (PathHunter® Flash Detection Kit, DiscoveRx; 93-0247) per well. After one hour of incubation at room temperature in the dark, the luminescence signal was measured on a plate reader (Envision®, Perkin Elmer). Raw

data were normalized to percentage activity values using the equation: 100 × (Sample – Negative control)/(Positive control – Negative Control) .

Table XVII.

Ingredient	**Final concentration in medium**	**Provider**	**Cat#**
BSA	0.5 mg/mL	Sigma	A7638
bovine pituitary extract	10 µg/mL	Sigma	P1476
Insulin	0.87 µM	Sigma	I9278
transferrin	0.125 µM	Sigma	T0665
hydrocortisone	0.21 µM	Sigma	H0396
triiodothyronine	0.01 µM	Sigma	T6397
Epinephrine	0.01 µM	Sigma	E4250
epidermal growth factor	5 ng/mL	Invitrogen	PHG0313
All-trans retinoic acid	5×10^{-8} M	Sigma	R-2625
o-Phosphoethanolamine	0.5 µM	Sigma	P-0503
ethanolamine	0.5 µM	Sigma	E0135
zinc sulfate (ZnSO4 · 7H2O)	3.0 µM	Sigma	Z0251
pen/strep	100 U/mL	Sigma	15140-122
ferrous sulfate	1.5×10^{-6} M	Sigma	F8048
magnesium chloride hexahydrate	6 × 10–4	Sigma	M2670
calcium chloride dihydrate	1.1×10^{-4} M	Fluka	21097
Trace elements:	-		
sodium selenite	30 nM	Sigma	S5261
manganese chloride tetrahydrate	1 nM	Sigma	M8054
sodium metasilicate nonahydrate	500 nM	Sigma	S5904
ammonium molybdate tetrahydrate	1 nM	Sigma	M1019
ammonium metavanadate	5 nM	Sigma	398128
nickel(II)sulfate hexahydrate	1 nM	Fluka (Sigma)	72280 (N4882)
tin(II) chloride dihydrate	0.5 nM	Sigma	243523

Measuring CFTR cell surface levels using HRP-tagged ΔF508-CFTR expressing CFBE cells

[00801] The HRP-tagged ΔF508-CFTR cell assay measures the expression of CFTR-ΔF508 at the plasma membrane. CFTR-ΔF508 has a folding defect leading to absence of protein at the plasma membrane. This assay is used to evaluate the capacity of compounds to increase the expression of CFTR-ΔF508 at the plasma membrane. The CFTR-ΔF508 is tagged with HRP (horse radish peroxidase enzyme) within the ECL4 (Extracellular loop 4) of CFTR (Phuan, P.-W. *et al.* Synergy-based small-molecule screen using a human lung epithelial cell line yields ΔF508-CFTR correctors that augment VX-809 maximal efficacy. *Mol. Pharmacol.* 86, 42–51 (2014)). When HRP-tagged ΔF508-CFTR is present at the plasma membrane, the HRP enzyme activity can be measured. The amount of CFTR-ΔF508 that can be rescued to the plasma membrane is correlated with the amount of functional enzyme that can be measured.

[00802] There are several ways to measure the capacity of compounds to rescue CFTR-ΔF508 to the plasma membrane; either compounds are evaluated on their own and the impact on plasma membrane levels is measured or compounds are evaluated in combination with a co-corrector, i.e. a compound that rescues CFTR-ΔF508 to the plasma membrane but rescue can be enhanced by addition of compounds due to a complementary mode of action.

Activity of compounds in combination with co-corrector:

[00803] For this purpose doxycycline-inducible ΔF508-CFTR-HRP expressing CFBE41o– cells (obtained from Gergely Lukacs, McGill University) were maintained in MEM (Minimum Essential Medium, Gibco; 31095) supplemented with 10% fetal bovine serum (Hyclone; SV30160.03) under puromycin (3 μg/mL) and G418 selection (0.2 mg/mL). For compound testing, cells were seeded at 4000 cells/well in white 384-well plates (Greiner; 781080) in 50 μL of medium containing 0.5 μg/mL doxycycline and incubated for 68 hours at 37 °C, 5% CO_2. On day four, 10 μL of test compounds diluted in PBS (phosphate buffered saline) were added to the plates at a final DMSO concentration of 0.1%. In order to measure compound synergy with a co-corrector, 3 μM co-corrector (3-[(2*R*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-7-methoxy-3,4-dihydro-2*H*-chromen-2-yl]benzoic acid) was added along with test compounds. All compound plates contained negative controls (DMSO) and positive controls (3 μM co-corrector). Cell plates were incubated at 33 °C, 5% CO_2 for 20 hours. On day five, the cells were washed five times with phosphate-buffered

saline, and HRP activity was assayed by the addition of 50 µL/well of HRP substrate (SuperSignal™ West Pico Chemiluminescent Substrate, Thermo Scientific; 34080). After incubation for 15 minutes in the dark, the chemiluminescence was measured using a plate reader (EnVision®, Perkin Elmer). Raw data were normalized to percentage activity values using the equation: 100 × (Sample – Negative control)/(Positive control – Negative Control).

Table XVIII. Illustrative EC_{50} measured by CFTR cell surface levels using HRP-tagged ΔF508-CFTR expressing CFBE cells in the presence of a co-corrector.

Compound #	% Activation	EC_{50} (nM)
1	297.2	1186
2	431.5	1122
4	405.8	297.9
5	362.75	371.75
6	387.1	510.7
7	420.63	554.03
8	441.85	853.8
9	335	505.05
10	606.5	442.65
11	381.33	455.35
12	364.15	713.8
13	341.75	1471
14	335.6	1368
15	346.15	852.15
16	649.9	458.65
17	320	1120
18	217.8	1110
19	304.05	1632.5
20	417.5	545.9
21	440.1	525.3
22	371.55	502.6

Compound #	% Activation	EC_{50} (nM)
23	468.85	573.35
24	380.5	743.95
25	437.17	640.17
26	449.7	1548
27	365.2	714
28	354.45	942.15
29	591.4	823.7
30	580.97	215.37
31	423.27	203.8
32	526	234
33	315.6	470.95
34	462.55	355.9
35	509.7	348.4
36	572.93	245.77
37	457.25	1163.1
38	447.7	581.23
39	378.63	507.77
40	373.43	422.67
41	253.3	1141
42	226.3	378.5
43	627	289.4

Compound #	% Activation	EC_{50} (nM)
44	412.63	276.27
45	438.4	202.94
46	643.27	445.83
47	408.77	1604.3
48	417.8	1152.5
49	338	1996.7
50	300	1075.5
51	420.67	311.5
52	257.85	992.4
53	572.78	647.2
54	593.12	463.62
55	341.65	1047.4
56	336.75	838.1
57	440	657.2
58	352.5	421.8
59	534.8	482.5
60	323.63	351.47
61	415.3	506.2
62	631.2	531.8
63	368.48	285.56
64	362.45	443.65
65	332.05	463.55
66	332.85	6670
67	371.62	241.18
68	456.6	847.1
69	362.03	403.63
70	342.85	409.6
71	447.8	263.55
72	400.9	5611

Compound #	% Activation	EC_{50} (nM)
73	423.35	490.05
74	424.82	357.1
75	387.16	290.54
76	581.37	632.67
77	449.85	831.2
78	520.7	660.5
79	501.6	555
80	457.5	389.5
81	646.44	253.16
82	535.93	383.03
83	567.7	424.5
84	468.2	408.1
85	570.16	232.1
86	489.56	255.04
87	623.62	456.46
88	546.2	412.73
89	609.48	396.26
90	384.95	388.85
91	619.45	890.95
92	367.67	278.4
93	456.5	270.4
94	421.53	341.9
95	611.7	649.15
96	707.5	473.05
97	692.82	277.25
98	360.15	393.3
99	601.15	336.8
100	340.6	3221
101	455.4	409.2

Compound #	% Activation	EC_{50} (nM)
102	458.75	536.55
103	501.03	409.03
104	411.33	344.37
105	457.85	698.9
106	348.1	393.95
107	219.4	3340
108	428.3	509.45
109	571.3	634.1
110	665.7	336.37
111	596.8	377.83
112	472.8	884.2
113	455.63	235.17
114	277.45	951.6
115	389.6	664.65
116	438.37	630.5
117	417.92	200
118	469	280
119	389.93	331.37
120	351.03	347.9
121	368.6	281.8
122	405.9	280.57
123	365.8	238.9
124	447.23	312.03
125	520.33	463.17
126	487.53	322.17
127	449.1	251.85
128	529.57	251.93
129	307.3	790.25
130	496.9	540.3

Compound #	% Activation	EC_{50} (nM)
131	465.1	580.65
132	417.2	881.65
133	417.7	335.87
134	435.8	236.8
135	512.9	373.43
136	428.1	72.26
137	339.7	638.35
138	433.83	235.77
139	335.5	764.83
140	377.9	380.65
141	414.63	221.37
142	376.93	78.407
143	217.8	833.55
144	674.7	242.99
145	271.43	636.17
146	357.55	96.872
147	363.93	99.92
148	448.03	169.85
149	299.95	259.05
150	380.65	318.29
151	387.15	108.87
152	409.9	107.85
153	290.05	130.35
154	447.85	203.45
155	555.45	229.66
156	636.47	360.2
157	542.17	358.74
158	512.45	266.75
159	270.3	483.27

Compound #	% Activation	EC_{50} (nM)
160	490.4	201.8
161	574.1	354.83
162	331.53	304.16
163	342.3	111.91
164	492.45	387.6
165	534.2	884.65
166	408.53	309.97
167	429.4	81.765
168	581.55	409.8
169	519.3	284.36
170	425.6	721.7
171	289.23	312.2
172	462.4	207.07
173	183.2	432.9
174	545	468.45
175	461.1	200.23
176	390.43	208.64
177	263.9	385.45
178	381.73	231.52
179	248.85	405.85
180	290.53	300.17
181	357.93	435.4
182	397.6	258.1
183	498.57	213.78
184	282.7	574.4
185	546.7	145.09
186	381.87	530.53
187	308.87	69.253
188	405.37	159.6

Compound #	% Activation	EC_{50} (nM)
189	409.6	236.27
190	502.4	1240.4
191	317.93	161.26
192	254.6	865.7
193	341.37	589.17
194	427.45	370.65
195	387.47	191.69
196	387.1	231.43
197	390.8	193.94
198	321.57	465.7
199	304.63	316.4
200	318.27	94.83
201	379.9	292.47
202	299.4	254.83
203	224.63	328.1
204	288.6	490.35
205	416.4	856
206	387.03	890.4
207	284.87	174.71
208	419.15	363.65
209	393.6	230.87
210	390.57	173.74
211	288.3	292.9
212	290.43	324.03
213	469.6	336.5
214	250.55	383.85
215	569.35	47.87
216	456.1	299.5
217	418.27	257.13

Compound #	% Activation	EC_{50} (nM)
218	476.9	238.67
219	524.4	230.26
220	389.9	207.87
221	492.2	77.24
222	247.3	1788.2
223	438.2	371
224	453.1	482
225	427.95	578.55
226	392.95	386.1
227	378.2	307.3
228	395.1	334.9
229	418.65	366.1
230	440.1	179.98
231	329.9	518.2
232	199.75	1726.5
233	206.57	1925.3
234	128.3	>10000
235	257.55	2485
236	497.5	93.19
237	264.05	222.18
238	347.55	218.6
239	431.55	1235.2
240	312.8	138.7
241	488.15	82.165
242	459.15	202.77
243	204.1	3330
244	290.6	413.5
245	460	693.6
246	331.65	77.25

Compound #	% Activation	EC_{50} (nM)
247	281.7	220.67
248	450.6	221.44
249	468.15	231.26
250	440.4	372
251	488.7	367
252	310.75	1691
253	454.4	250.85
254	312.1	370
255	365.8	3330
256	508.63	147.3
257	451.25	74.3
258	127.1	>10000
260	664.07	129.88
261	129.3	>10000
262	420.17	523.02
263	475.45	403.78
264	478.6	3330
265	427.8	2138
266	328.87	230.63
267	433	57.095
268	122.05	>10000
269	275.45	97.25
270	327.9	730.83
271	260.47	1016.5
272	451.2	43.33
273	344.05	111.1
274	300	398.1
275	269.85	138
276	417.25	42.905

Compound #	% Activation	EC_{50} (nM)
277	355.4	127.1
278	388.5	88.315
279	530.6	227.4
280	323.37	1010.2
281	398.47	242.33
282	379.95	89.015
283	326.85	265.5
284	348.7	219.8
285	327.57	246
286	500.55	158.6
287	450.9	128.29
288	566.4	74.34
289	366.4	3330
290	382.2	535.7
291	420.07	590.9
292	422.55	564.7
293	317.1	479.7
294	548.45	22.065
295	298.07	697.2
296	329.13	167.8
297	423.43	77.2
298	481.2	81.025
299	267.2	2514.5
300	266.55	109.26
301	376.6	1136.4
302	401.45	1799.6
303	339.95	834.25
304	507	56.145
305	267	2443

Compound #	% Activation	EC_{50} (nM)
306	321.1	82.395
307	299.25	1278.8
308	328.85	2492.5
309	303.6	224.05
310	251.5	923.65
311	241.35	1060.6
312	291.5	1882.5
313	319.75	1749
314	375.8	693.1
315	315.5	101.55
316	555.55	24.4
317	450.35	48.825
318	359.5	184.25
319	232	979.57
320	590.6	82.663
321	314.37	496.53
322	342.75	61.415
323	292.85	372.05
324	259.7	1635.4
325	309.8	152.6
326	325.3	729.7
327	433.9	99.9
328	554.2	185.7
329	318.4	777.1
330	285.4	124.3
331	546.05	38.185
332	448.25	624.3
336	232.42	282.15
337	532.3	30.55

Compound #	% Activation	EC_{50} (nM)
338	344.25	945.55
339	295.5	402.1
340	319.2	785.8
341	165.4	3330
342	336.5	207.1
343	356.9	566.3
344	374.5	1061
345	301.1	222.8
346	375.1	253.45
347	301.15	54.26
348	468.65	723.5
349	327.9	424.45
350	274.6	286.95
351	232.5	81.07
352	158.4	2778
353	193.45	346.44
354	351	232.2
355	278.4	377.1
356	372	48.27
357	229.8	129.5
358	242.33	89.854
359	236.25	298.9
360	182.8	100.72
361	204.1	181.2
362	195.75	413.8
363	415.8	116.2
364	575	553
365	469.95	271.05
366	443.7	82.67

Compound #	% Activation	EC_{50} (nM)
367	526.17	81.56
368	350.23	361
369	444	105.88
370	343.2	691.05
371	271.9	1926.5
372	615.7	2560
373	580.5	85.76
374	426.05	195.67
375	546.75	241.45
376	496.8	51.61
377	485.55	102.74
378	318.6	657.55
379	440.55	61.09
380	309.17	127.16
381	432.09	155.99
382	500.01	158.29
383	412.20	94.26
384	391.35	1443
385	393.53	64
386	385.05	684.75
387	168.9	160.7
388	364.5	195.93
389	305.1	297.3
390	350.17	139.8
391	441.15	85.535
392	421.4	138.66
393	533.65	20.77
394	366.87	47.877
395	327.95	126.69

Compound #	% Activation	EC_{50} (nM)
396	385.8	55.037
397	381.8	48.963
398	324.03	73.623
399	388.77	44.157
400	365.43	156.83
401	595.1	61.98
402	471.42	116.35
403	507.35	25.628
404	370	125.8
405	326.9	101.86
406	311.35	181.65
407	494.15	124.02
408	466.58	199.45
409	481.1	108.14
410	529.58	82.442
411	505	478.2
412	436.4	200.6
413	455.9	90.59
414	508.3	158.6
415	598	69.31
416	458.65	64.97
417	539.75	91.905
418	512.9	220.8
419	505.65	277.1
420	486.65	209.2
421	512.9	124.75
422	434.33	204.27
423	376.85	108.84
424	453.88	92.203

Compound #	% Activation	EC_{50} (nM)
425	462.85	166.45
426	385.3	82.03
427	419.5	162.5
428	434.7	77.27
429	422.8	205.15
430	383.7	89.87
431	568.8	47.003
432	514.83	65.943
433	563.8	49.01
434	470.37	59.51
435	474.8	82.825
436	568.6	71.07
437	563.64	155.81
438	541.5	380.5
439	374.6	381
440	543.55	55.44
441	393.27	196.47
442	342	1110
443	332.5	183.9
444	361.3	235.1
445	671.25	59.11
446	669.9	77.435
447	543.1	64.69
448	431.1	180.75
AC07	466.9	76.57
450	443.25	246.25
451	391	2102
452	478.25	941.8
453	385.1	319

Compound #	% Activation	EC_{50} (nM)
454	430.2	639.4
456	457.7	93.273
457	508	139.41
458	282.8	920.4
459	388.87	96.053
460	306.75	505.05
461	364.1	177.2
462	495.1	106.85
463	490.6	194.5
464	423.3	170.38
465	293.15	360.35
466	522.47	64.097
467	229.15	270.35
468	443.05	524.2
469	469.4	125.4
470	485.5	114.8
471	446.07	122.4
472	399.79	249.47
473	370.7	43.935
474	390.2	524.45
475	289.95	112.32
476	355.65	151
477	536.7	34.725
478	476.7	126.64
479	524.1	108.95
480	545.77	87.11
481	285.65	154.25
482	436.4	61.63
483	438.2	56.15

Compound #	% Activation	EC_{50} (nM)
484	485.6	142.1
485	399.1	90.217
486	569	180.5
487	404.63	68.97
488	488.15	682.55
489	280	241.2
490	303.9	692.6
491	490.9	487.8
492	483.4	43.91
493	480.78	94.585
494	551.8	37.085
495	469.08	66.152
496	374.65	242.9
497	378.25	287.65
498	456.3	95.12
499	439.6	71.165
500	330.05	84.215
501	403.55	124.3
502	383.8	176.9
503	433.2	404.7
504	404.8	210.05
505	389	54.11
506	308.95	941.25
507	580.4	95.4
508	448.8	90.31
509	527.9	118.4
510	428.8	170.9
511	432.95	78.94
512	415.25	65.265

Compound #	% Activation	EC_{50} (nM)
513	476.3	66.74
514	540.3	97.07
515	479.2	52.88
516	545.3	56.56
517	520.08	75.79
518	189.55	3125.5
519	252.3	1023.3
520	207.1	923.7
521	217.3	711.5
522	525.66	79.788
523	451.33	100.04
524	398.75	307.55
525	460.3	73.968
526	472.58	106.56
527	500	53.775
528	357.9	834.45
529	444.13	22.557
530	464.6	22.955
531	349.65	63.465
532	342.83	472.67
533	322.45	220.95
534	289.35	344.1
535	670.35	1251.9
536	341.15	280.1
537	417.1	50.845
538	427.95	357.55
539	429.3	38.63
540	443.3	102.59
541	457.2	114.95

Compound #	% Activation	EC_{50} (nM)
542	320.3	216.1
543	336.1	139.25
544	344.9	1996.4
545	318.7	1905.4
546	335.3	181.9
547	372.95	348.5
548	556.9	553.5
549	476.35	180.4
550	605.45	173.15
551	403.1	382.3
552	364.2	130.43
553	494.3	233.25
554	481	56.86
555	432.55	104.12
556	595.8	136.2
557	474.4	116.35
558	571.35	106.46
559	291.03	154.3
560	544.45	66.1
561	509.4	43.023
562	589.55	77.645
563	542.9	111.13
564	587.4	40.75
565	637.53	69.86
566	708.8	400.42
567	539.8	56.343
568	461	46.295
569	436.13	88.907
570	412.9	208.3

Compound #	% Activation	EC_{50} (nM)
571	487.9	77.77
572	412.9	225.1
573	467.57	58.533
574	283.3	541.9
575	361.3	87.8
576	443.5	54.673
577	379.3	104.7
578	462.3	107.6
579	420.5	318.8
580	387.45	52.425
581	191.3	760.8
582	245.15	271.05
583	480.15	47.595
584	337.55	272.35
585	509.7	247.75
586	618.65	37.12
587	504.6	398.2
588	571.2	29
589	422.95	148
590	487.9	31.395
591	384	1592
592	518.55	56.8
593	366.7	193.7
594	308.05	181.45
595	231.9	1430
596	304.8	1908
597	433.93	110.63
598	153.9	10000
599	285.2	269.7

Compound #	% Activation	EC_{50} (nM)
600	326.1	1618
601	273.9	625
602	359.1	581.4
603	344.65	156.3
604	268.3	300
605	395.8	723
606	513.7	468.6
607	484.3	667.1
608	365.7	54.765
609	414.2	108.91
610	375.5	118.72
611	236.7	2620
612	320.8	3330
613	152.9	10000
614	381.35	170.65
615	450.85	130
616	341.15	294.35
617	324.25	978.45
618	295.9	702.35
619	277.25	374.7
621	348.55	76.95
622	251.25	308.6
623	424.77	55.623
624	274.15	549.2
625	353.87	125.87
626	418.4	111.06
627	348.57	24.793
628	477.32	131.66
629	546.75	266.92

Compound #	% Activation	EC_{50} (nM)
630	593.42	374.58
631	352.63	2986.2
632	466.83	153.9
633	400.44	206.9
634	439.44	78.79
635	449.25	73.852
636	388.85	434.18
637	413.4	971.25
638	606.08	95.005
639	464.55	74.532
640	416.48	107.31
641	443.12	46.265
642	430.9	97.285
643	445.25	496.82
644	529.95	160.16
645	384.37	244.21
646	447.9	259.12
647	337.07	112.2
648	288.85	110.15
649	231.7	152.35
650	592.45	96.375

Compound #	% Activation	EC_{50} (nM)
651	532.4	127.6
652	499.65	24.855
654	347.6	114.46
656	289.68	71.475
657	270.75	196.82
658	270.6	148.53
659	290.95	130.45
660	172.1	235.5
661	227.45	135.34
662	346.65	104.39
663	206.5	102.86
664	230.48	172.5
665	271.8	100.86
666	266.6	121.58
667	225.5	85.485
668	307.4	257.2
669	394	244.4
670	477.6	191.3
671	346.1	107
672	422.4	127.3

Activity of compounds for their intrinsic corrector capacity:

[00804] For this purpose doxycycline-inducible ΔF508-CFTR-HRP expressing CFBE41o− cells (obtained from Gergely Lukacs, McGill University) were maintained in MEM (Gibco; 31095) supplemented with 10% fetal bovine serum (Hyclone; SV30160.03) under puromycin (3 µg/mL) and G418 selection (0.2 mg/mL). For compound testing, cells were seeded at 4000 cells/well in white 384-well plates (Greiner; 781080) in 50 µL medium containing 0.5 µg/mL doxycycline and incubated for 68 hours at 37 °C, 5% CO_2. On day four, 10 µL test compounds diluted in PBS were added to the plates at a final DMSO concentration of

0.1%. All compound plates contained negative controls (DMSO) and positive controls (3μM corrector, 3-[(2*R*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-7-methoxy-3,4-dihydro-2*H*-chromen-2-yl]benzoic acid). Cell plates were incubated at 33 °C, 5% CO_2 for 20 hours. On day five, the cells were washed five times with phosphate-buffered saline, and HRP activity was assayed by the addition of 50 μL/well of HRP substrate (SuperSignal™ West Pico Chemiluminescent Substrate, Thermo Scientific; 34080). After incubation for 15 minutes in the dark, chemiluminescence was measured using a plate reader (EnVision®, Perkin Elmer). Raw data were normalized to percentage activity values using the equation: 100 × (Sample – Negative control)/(Positive control – Negative Control) .

Table XIX. Illustrative EC_{50} measured by CFTR cell surface levels using HRP-tagged ΔF508-CFTR expressing CFBE cells.

Compound #	% Activation	EC_{50} (nM)
1	138.85	1628.9
2	226.75	1867
3	53.08	3340
4	246.7	838.35
5	184.6	476.6
6	232.1	808.3
7	245	636
8	270.6	899.55
9	143.05	785.9
10	418.25	572.5
11	164.7	556.52
12	161.15	1072.5
13	153.85	2361
14	148.9	1429.5
15	151.65	1192.5
16	469.75	543.05
17	140.75	1225.5

Compound #	% Activation	EC_{50} (nM)
18	64.675	2267
19	140.85	2652.5
20	210.3	669.15
21	264.25	685.3
22	161.5	731.65
23	287.3	883.5
24	193.75	887.75
25	247.23	996.8
26	202.25	1847.5
27	145.5	1219
28	149.7	1218
29	328.4	645.05
30	369.93	436.27
31	203.4	318.2
32	277.65	372.25
33	109	2578.5
34	292.95	610.75

Compound #	% Activation	EC_{50} (nM)
35	265.23	542.1
36	384.57	415.9
37	222.85	1662
38	182	849.97
39	143.4	838.2
40	147.1	450.97
41	52.497	816.53
42	45.225	2123
43	379.67	299.47
44	203.87	404.4
45	210.97	326.73
46	457.3	706.07
47	169.73	1862
48	160.9	1195.9
49	115.3	2566.7
50	109.8	1683.5
51	172.4	456.57
52	75.755	1153
53	376.8	671.1
54	386.92	779.92
55	126.75	1220.2
56	122.1	1177
57	219.65	1024.5
58	196.2	756.33
59	317.3	777.47
60	160.43	394.4
61	184.35	1003
62	350.85	595.75
63	179.68	548.28

Compound #	% Activation	EC_{50} (nM)
64	152.75	935.35
65	162.33	1532.5
66	142.65	1861.4
67	181.96	361.86
68	253.3	1079
69	182.08	631.68
70	167.8	621.35
71	260.66	350
72	232.5	2226.5
73	254.1	657.45
74	253.38	549.12
75	225.82	489.92
76	430.87	528.07
77	296.45	639
78	333.2	1878.3
79	280.9	1227
80	258.38	436.18
81	495.8	384.52
82	366.27	472.07
83	391.5	547.1
84	311.7	659.8
85	426.04	420.84
86	329.92	637.3
87	422.84	408.78
88	389.73	474.4
89	422.78	645.7
90	163.75	485.6
91	388.15	381.7
92	175.77	552.8

Compound #	% Activation	EC_{50} (nM)
93	224.23	501.2
94	193.5	614.33
95	355.6	837.85
96	406.6	366.9
97	444.85	399.2
98	154	555.55
99	414.8	409.65
100	113	2475
101	254.85	838.65
102	233.9	897.2
103	263.8	535.87
104	239.6	496.9
105	258.1	908.4
106	162.75	525.9
107	64.54	3340
108	218.05	560.55
109	381.05	612.85
110	451.8	358.13
111	411.63	444.3
112	254.85	699.5
113	262.33	464.4
114	130.85	1136
115	216.05	1050
116	295.57	957.23
117	281.88	332.78
118	289.93	397.63
119	188.53	519.5
120	169.2	553.7
121	159.13	652.53

Compound #	% Activation	EC_{50} (nM)
122	184.53	469.67
123	153.8	428.27
124	288.1	544.77
125	369.87	988.13
126	309.17	597.03
127	301.45	517.9
128	357.47	515.83
129	187.5	1326.5
130	318.25	541.35
131	314.35	429.85
132	244	1270.5
133	222.33	412.87
134	229.87	465.2
135	299.63	695.8
136	262.38	154.65
137	131.8	1173.2
138	252.9	333.73
139	163.83	806.07
140	210.3	733.5
141	233.07	287.2
142	203.17	254.9
143	107.15	1110
144	531.6	416.52
145	112.03	1039.4
146	201.23	356.08
147	176.47	358.63
148	273.33	547.73
149	122.3	385.75
150	220.98	576.45

Compound #	% Activation	EC_{50} (nM)
151	228.95	346.65
152	242.35	357.15
153	146.7	354.95
154	275.65	532.9
155	439.5	454.35
156	411	438.63
157	327.8	460.03
158	359.1	622
159	103.02	661.2
160	285.57	309.47
161	406.4	729.53
162	169	445.43
163	175.4	441.8
164	295.25	594.45
165	373.95	1781
166	235.2	439.43
167	260.6	313.35
168	399.2	338.2
169	344.25	426.22
170	213.5	974.85
171	143.4	787.07
172	280.03	329.77
173	51.395	412.4
174	347.9	753.6
175	270.5	337.5
176	190.4	337.3
177	99.405	829.6
178	202.8	346.9
179	89.165	878.85

Compound #	% Activation	EC_{50} (nM)
180	129.5	570.07
181	137.73	397.87
182	207.57	501.43
183	302	389.5
184	95.405	719.25
185	331.6	241.45
186	209.57	616.13
187	160	223.43
188	214.93	274.5
189	236.2	420.6
190	284.8	966.55
191	161.23	305.6
192	81.49	1135
193	175.23	1067.5
194	213.75	744.5
195	225.2	369.7
196	188.47	339.43
197	220.2	397
198	135.73	632.97
199	142.6	481.47
200	163.43	315.7
201	200.8	402.17
202	147.23	595.43
203	82.59	1015.5
204	117.6	977.95
205	208.5	955.55
206	169.03	1396.1
207	141.93	339.73
208	190.55	402.45

Compound #	% Activation	EC_{50} (nM)
209	247.6	380.97
210	205.57	285.6
211	114.4	608.15
212	114.63	620.9
213	267.5	546.25
214	103.6	1010.8
215	374.57	274.4
216	275.67	765.67
217	246.77	458.47
218	268.37	390.4
219	381.1	764.1
220	202.5	347.9
221	322.15	420.05
222	65.685	1423.2
223	258.95	469.5
224	228.8	544.2
225	215.35	456.25
226	206.7	445.05
227	216.8	448.6
228	217.9	489.9
229	174.2	414.1
230	243.75	406.1
231	162.9	939.25
232	71.64	1678
233	58.34	2438
234	17.89	>10000
235	102.76	3271
236	309.83	316.47
237	120	453.2

Compound #	% Activation	EC_{50} (nM)
238	159.83	600.57
239	184.6	999.25
240	176.67	376.63
241	261.93	366.43
242	242.1	282.83
243	78.11	3340
244	182.7	381.2
245	228	495.1
246	112.1	371
247	126.8	460
248	234.6	371
249	187.6	371
250	232.7	514
251	273.3	634
252	115.2	396.5
253	174.6	675.6
254	117.5	399.8
255	122.3	1881
256	331.85	220.65
257	272.4	370
258	8.829	>10000
260	473.35	1868.6
261	26.85	>10000
262	232.07	597.87
263	260.1	444.83
264	242.5	969.2
265	240.8	3330
266	161.5	332
267	274.8	171.6

Compound #	% Activation	EC_{50} (nM)
268	5.213	>10000
269	120.6	246.4
270	161.5	1493
271	63.905	1952
272	268.2	96.55
273	182.4	562.4
274	159.05	842.5
275	138.8	467.7
276	356.7	779.3
277	155.4	251.1
278	233.7	119.5
279	308.4	533.7
280	121.9	1007
281	230.15	456.5
282	127.8	129.3
283	141.2	477
284	154.4	275.7
285	125.5	293.8
286	264	326.8
287	204.9	183.2
290	200.4	617.4
291	219.5	3330
292	217.9	1057
293	113.3	622.2
294	319.6	62.24
295	129.6	1052
296	154.7	396.5
297	193.9	99.18
298	312.9	282.1

Compound #	% Activation	EC_{50} (nM)
299	81.41	3330
300	119.9	309.4
303	149.9	3330
304	308.2	202.9
306	146.7	157.7
307	172.7	3330
309	149	444.3
310	66.84	691.9
315	154.87	218.03
316	380.5	182.8
317	269.6	93.52
318	183.45	411.25
319	34.315	297.7
320	376.35	309.35
322	158.25	128.05
323	144.6	1366
325	151.4	334.8
326	167.1	2384.5
327	239.4	145.2
328	380.5	2186
329	163.85	158.2
330	133.1	213.45
331	347.15	136.25
333	180	82.765
334	121.75	167.4
335	171.65	149.85
336	107.2	419.9
337	404.9	133.58
339	142.05	1401

Compound #	% Activation	EC_{50} (nM)
340	138.95	1392
346	195.8	308.2
347	131.4	263
348	293.6	5969.5
349	161.7	512.3
350	104.21	357.15
351	50.87	73.45
352	27.44	5000
353	56.22	87.86
354	113.7	122.9
355	102.4	160.5
356	188.25	105.3
357	72.83	115.2
365	313	1670
366	264	297.9
367	364.5	311.4
368	185	1359
369	292.7	100.6
370	172.2	1490
371	121.3	2744
373	368.2	72.97
374	240.7	254.3
375	321.6	570.9
376	355.7	117.4
377	261.3	129
378	160	1327
379	268.45	141.1
380	131.7	279.3
381	247.15	424.06

Compound #	% Activation	EC_{50} (nM)
382	305.9	260.6
383	202.9	149.8
384	228	2862
385	227.5	120.95
386	237.85	2116
387	60.58	462
388	192.8	217.9
389	165	556.1
390	188.2	176.9
391	247.7	77.1
392	240.05	150.45
393	423.6	51.37
394	194.35	99.53
395	209.2	473.8
396	222.9	121.35
397	234.5	154.55
398	173.7	181.5
399	237.5	72.075
400	180.65	163.05
401	400.8	104.1
402	303.5	312.28
403	389.2	30.18
404	181.2	185.6
405	160.8	190.7
406	125.95	240.8
407	331.45	496.9
408	272.74	689.62
409	245.4	154.9
410	337.42	212.87

Compound #	% Activation	EC_{50} (nM)
415	365.4	165.4
416	288	141.9
417	307.45	189.7
418	321.3	320.9
419	293	448.1
420	283.1	472
421	308	250.1
422	222.8	318.5
423	175.55	140.1
424	249.25	244.25
425	280.2	277.1
426	143.7	301.6
429	252.1	378
430	170.05	231.3
431	344.95	109.3
432	243.6	118.5
433	361.5	96.46
434	245.2	57.74
435	269.9	135.9
436	393.3	344
437	353.8	257
438	337	391.8
439	166.8	550
440	334.8	129
441	196.1	350
442	146.8	307.3
444	162.5	344.7
445	393.1	110.7
447	330.9	243.5

Compound #	% Activation	EC_{50} (nM)
448	258.2	476.9
AC07	268.5	139.5
450	253.5	617.5
451	184.1	1698
452	239.8	408.4
453	149.3	403
454	168.1	1670
456	268.4	157.7
457	272.2	128.5
458	124.4	794.4
459	225.65	148.95
460	125.8	595.6
461	212.3	209.4
462	317.4	775.5
463	263.9	419.1
464	277.5	306.3
465	131.6	312.8
466	318.7	175.8
469	253.8	203.9
470	275.4	231.1
471	240.2	230.2
472	210.57	680.74
473	166.3	70.76
474	194.5	580.5
475	140.1	178.8
476	134.2	215
477	341.4	117
478	295.4	2639
479	305.7	196.6

Compound #	% Activation	EC_{50} (nM)
480	322.45	135.7
481	114.2	278.1
482	214.1	88.17
483	212.7	84.88
484	216.9	124.3
485	218.55	155.15
486	332.5	467.3
487	203.53	174.87
488	246.55	655.45
489	99.6	141.5
490	139.7	1546
491	204.5	248.3
492	311	79.93
493	275.2	174.6
494	315.4	109.8
495	242.05	217.1
496	199.9	281.8
497	195.7	410.4
498	288.1	144.3
499	287.5	186.4
500	137.5	173.5
501	188.7	210.7
502	214.2	345.4
503	203.4	418.8
504	206.4	300.8
505	187.5	92.57
506	144.1	3330
507	309.4	136.8
508	217.5	182.2

Compound #	% Activation	EC_{50} (nM)
509	333.2	326.6
510	234.9	297.6
511	248.55	88.31
512	222.27	120.97
513	278.5	100.5
514	301.4	149.8
515	287.1	179.2
516	322.7	120.2
517	320.5	183.95
518	35.86	10000
519	114.4	3330
520	60	1056
521	31.93	10000
522	317.9	114.21
523	236.53	123.6
524	209.35	525
525	274.75	137.75
526	269.23	152.72
527	295.95	79.095
528	185.8	859.1
529	278.55	60.605
530	323.1	54.43
531	182.8	234.05
532	151.95	521.25
533	156.3	221.85
534	105	240.7
535	385.8	389
536	125.1	224.8
537	214.5	112.2

Compound #	% Activation	EC_{50} (nM)
538	228.9	2073
539	234.5	71.71
540	248.8	123.3
541	231.7	444.2
542	153.2	266.8
543	115.7	238.2
544	135.3	3330
545	112.7	3330
546	138.05	325.2
548	307.2	654.3
549	276.9	232.9
550	347	361
551	197.8	763.15
553	293	1732
554	269.45	108.15
555	235.5	358.77
556	386	64.67
557	248.5	252
558	399.1	531.6
560	260.4	96.34
561	311.6	107.08
562	341.3	70.505
563	298.9	198.3
564	361.35	117.81
565	373.15	181.8
566	365.1	112.3
567	312.2	139.4
568	240.65	77.465
569	220.77	112.18

Compound #	% Activation	EC_{50} (nM)
570	235.8	496.2
571	268.15	128.75
572	237.55	295.1
573	270.53	104.32
574	129.9	2756
575	202.65	147.4
576	257.15	139.41
577	187.15	256.6
578	309.25	152.15
579	205	375.87
580	201.52	130.88
581	33.38	370
582	75.38	370
583	269.7	178.2
584	164.3	176.7
585	316.6	1242
586	331.67	52.367
587	277.1	234.6
588	366.8	125.95
589	193.6	199.6
590	290.3	86.7
591	189.1	795.1
592	300.8	182.6
593	157.8	189.7
594	135.7	518.85
595	58.87	1519
596	104.3	1381
597	214.3	130.2
598	28.03	10000

Compound #	% Activation	EC_{50} (nM)
599	88.94	331.3
600	126.5	1213
601	112	2177
602	133.6	1177
603	136.2	282.7
604	86.51	490.4
605	207.5	317.5
606	283.8	973
607	272.6	342
608	194.67	103.52
609	202.53	249.1
610	182.13	185.8
611	77.39	3330
612	108.7	875.8
613	30.09	10000
614	172	211.3
615	255.3	482.5
616	144.05	348.1
617	137.1	871.25
618	112.8	420.6
619	102.8	680.25
621	160.45	172.9
622	89.445	568.4
623	238.53	112.73
624	100.59	1203.1
625	182.2	222.97
626	206.6	150.83
627	162.47	82.293
628	283.25	425.38

Compound #	% Activation	EC_{50} (nM)
629	337.34	517.05
630	339.64	738.66
631	122.53	3336.7
632	252.75	304.4
633	180.46	345.2
634	227.46	199.84
635	216.38	154.84
636	182.7	572.78
637	191.88	2502.2
638	398.98	241.05
639	238.35	131.92
640	203.62	174.7
641	205.35	74.852
642	222	234.88
643	181.65	505.98
644	266.9	253.35
645	194.33	331.1
646	236.13	400.12
647	164.47	215.73
648	109.65	315.7
649	69.12	370
650	385.4	115.06
651	317.85	205.75
652	289.03	84.117
654	73.925	5075.4
656	102.63	99.61
657	98	281.48
658	99.025	252.5
659	96.44	141.95

Compound #	% Activation	EC_{50} (nM)
660	34.92	932
661	67.125	154.65
662	134.35	123.75
663	57.9	234.35
664	70.082	277.62
665	101.9	259.35
666	99.775	255.6
667	75.435	208.1
668	89.495	384.5
669	334.9	211.35
670	399.2	276.75
671	252.95	273.5
672	362.9	330.9

Compound #	% Activation	EC_{50} (nM)
673	423.5	288.5
675	398.1	315.6
674	389.5	155.9
676	251.1	251.3
677	458.5	170.7
678	345.1	220.9
679	476.9	131.7
680	351.2	339.1
681	366.2	172
682	260.8	297.2
683	354.9	252.9
684	356.9	114.6
685	144.3	769.9

YFP-halide influx assay for the CFTR-ΔF508 mutation

[00805] The YFP halide influx assay measures the functionality of the Cystic Fibrosis Transmembrane Conductance regulator (CFTR) channels in the cystic fibrosis bronchial epithelium cell line CFBE41o-. The fluorescence of the yellow fluorescent protein (YFP) variant YFP H148Q, I152L or variant YFP H148Q, I152L & F47L is substantially quenched by iodine, a halide that is efficiently transported by CFTR. The assay is thus used to evaluate the effect of corrector compounds on CFTR channel function by measuring the extent of YFP signal quenching. (Galietta, L.J.V., Haggie, P.M., Verkman, A.S., 2001. Green fluorescent protein-based halide indicators with improved chloride and iodide affinities. FEBS Lett. 499, 220–224. doi: 10.1016/S0014-5793(01)02561-3; Nagai, T., Ibata, K., Park, E.S., Kubota, M., Mikoshiba, K., Miyawaki, A., 2002. A variant of yellow fluorescent protein with fast and efficient maturation for cell-biological applications. Nat. Biotechnol. 20, 87–90. doi: 10.1038/nbt0102-87). For this purpose, CFBE41o- cells were seeded in 96-well plates (6000 CFBE cells/well). One day after seeding, the CFBE cells were transduced with adenoviral vectors that direct the expression of the CFTR ΔF508 mutant and of the YFP reporter. Cells were treated with test

compounds for 24 hours at 37 °C to allow trafficking of corrected CFTR to the membrane. The next day the CFTR channels were activated by treatment with the cAMP inducer forskolin (10.67 μM) and potentiator, *N*-(3-carbamoyl-5,5,7,7-tetramethyl-4,7-dihydro-5*H*-thieno[2,3-*c*]pyran-2-yl)-1*H*-pyrazole-5-carboxamide (0.5μM), in 1×D-PBS (from Gibco, Cat n# 14090-091) for 20 minutes prior to addition of an I^- solution (137 mM NaI, 2.7 mM KI, 1.76 mM KH_2PO_4, 10.1 mM Na_2HPO_4, 5 mM glucose). The potentiator, 3-amino-*N*-[(2*S*)-2-hydroxypropyl]-5-{[4-(trifluoromethoxy)phenyl]sulfonyl}pyridine-2-carboxamide, was used in place of *N*-(3-carbamoyl-5,5,7,7-tetramethyl-4,7-dihydro-5*H*-thieno[2,3-*c*]pyran-2-yl)-1*H*-pyrazole-5-carboxamide in some assays. The I^- induced quenching of fluorescence is recorded immediately after injection of I^- for 7 seconds. The capacity of a compound to increase number of channels, and therefore overall halide influx is directly correlated with the decrease in fluorescence, and is expressed as (1- (fluorescence after 7 seconds (F)/fluorescence before injection (F0))) and an EC_{50} can be derived from a (1-F/F0) vs compound concentration plot.

TECC Assay

Primary bronchial epithelial cells Protocol

[00806] The TECC (Tranepithelial Clamp Circuit, EP-design) assay measures the functionality of the cystic fibrosis Transmembrane Conductance regulator (CFTR) by measuring the short circuit current (I_{SC}) generated over the basolateral and apical membrane of lung epithelial cells. In TECC the transepithelial potential PD and transepithelial resistance (R_t) are measured in an open circuit and transformed to I_{eq} using Ohm's law. 24 Wells can be measured simultaneously allowing a higher throughput compared to Ussing chambers.

[00807] For this purpose, bronchial epithelial cells isolated from CF patients homozygous for the CFTR ΔF508 mutation (hAEC-CF, Epithelix, Geneva, Switzerland; McGill University, Montreal, Qc; Asterand, Detroit, MI; University of North Carolina, Chapel Hill, NC) are plated on type IV collagen-coated Transwell® supports (Costar). Human airway epithelia are generated by provision of an air–liquid interface for 21 days to form well-differentiated polarized cultures that resemble in vivo pseudo-stratified ciliated epithelium (Fulcher, M.L., Gabriel, S., Burns, K.A., Yankaskas, J.R., Randell, S.H., 2005. Well-differentiated human airway epithelial cell cultures. Methods Mol. Med. 107, 183–206). The differentiated cells are treated with test corrector compound(s) (corrector alone or in combination with co-corrector, 4-[(2*R*,4*R*)-4-({[1-

(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-7-methoxy-3,4-dihydro-2*H*-chromen-2-yl]benzoic acid ("acute") or test corrector compounds, co-corrector and potentiator, *N*-(3-carbamoyl-5,5,7,7-tetramethyl-4,7-dihydro-5*H*-thieno[2,3-*c*]pyran-2-yl)-1*H*-pyrazole-5-carboxamide ("chronic") for 24 hours basolaterally to allow sufficient expression of properly folded CFTR protein on the membrane. All compound plates contained negative controls (DMSO) and positive controls (0.15µM, 4-[(2*R*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-7-(difluoromethoxy)-3,4-dihydro-2*H*-chromen-2-yl]benzoic acid).

[00808] For electrophysiological recording of the "acute" experiments, the human airway epithelia are mounted in the TECC heating plate and kept at 37 °C. The epithelia are bathed in a NaCl-Ringer solution (120 mM NaCl, 25 mM $NaHCO_3$,1.2 mM $CaCl_2$, 1.2 mM $MgCl_2$, 0.8 mM KH_2PO_4, 0.8 mM K_2HPO_4, pH 7.4, 5 mM glucose) on both the basolateral and apical sides. Apical amiloride is used to inhibit the endogenous epithelial sodium channel (ENaC) currents while forskolin is applied on both apical and basolateral side to stimulate CFTR. CFTR activity is measured by addition of forskolin followed by addition of a potentiator, *N*-(3-carbamoyl-5,5,7,7-tetramethyl-4,7-dihydro-5*H*-thieno[2,3-*c*]pyran-2-yl)-1*H*-pyrazole-5-carboxamide, on both sides. The potentiator, 3-amino-*N*-[(2*S*)-2-hydroxypropyl]-5-{[4-(trifluoromethoxy)phenyl]sulfonyl}pyridine-2-carboxamide, was used in place of *N*-(3-carbamoyl-5,5,7,7-tetramethyl-4,7-dihydro-5*H*-thieno[2,3-*c*]pyran-2-yl)-1*H*-pyrazole-5-carboxamide in some assays. Measurements are done during a 20 minute timeframe with recordings every 2 minutes. The increase in I_{eq} is used as a measure for the increased CFTR activity, EC_{50} values can be generated by measuring impact of different concentrations of compound on I_{eq} on primary cells, for this purpose each transwell is treated with a different compound concentration for 24 hours. Inhibitor-172, an inhibitor specific for CFTR, is used to test the specificity of the tested compounds. Raw data were normalized to percentage activity values using the equation: 100 × (Sample – Negative control)/(Positive control – Negative Control).

Table XX. Illustrative acute TECC assay response with and without the presence of a co-corrector.

Compound #	% Activity at	% Activity at	% Activity at 3 µM with

	3 μM (Ieq*)	10 μM (Ieq*)	co-corrector (Ieq*)
10	591.84		
11	351		
13	74.32	174.53	
104			102.36

*Ieq refers to calculations based on the maximum current.

[00809] For electrophysiological recording of the "chronic" experiments, the human airway epithelia are mounted in the TECC heating plate for electrophysiological measurement and kept at 37 °C. The epithelia are bathed in a NaCl-Ringer solution (120 mM NaCl, 25 mM $NaHCO_3$, 1.2 mM $CaCl_2$, 1.2 mM $MgCl_2$, 0.8 mM KH_2PO_4, 0.8 mM K_2HPO_4, pH 7.4, 5 mM glucose) on both the basolateral and apical sides. Test compounds (corrector, co-corrector, 4-[(2*R*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-7-(difluoromethoxy)-3,4-dihydro-2*H*-chromen-2-yl]benzoic acid, and potentiator, *N*-(3-carbamoyl-5,5,7,7-tetramethyl-4,7-dihydro-5*H*-thieno[2,3-*c*]pyran-2-yl)-1*H*-pyrazole-5-carboxamide), are re-added to the recording solution prior to measurement. The potentiator, 3-amino-*N*-[(2*S*)-2-hydroxypropyl]-5-{[4-(trifluoromethoxy)phenyl]sulfonyl}pyridine-2-carboxamide (1.5 μM) , was used in place of *N*-(3-carbamoyl-5,5,7,7-tetramethyl-4,7-dihydro-5*H*-thieno[2,3-*c*]pyran-2-yl)-1*H*-pyrazole-5-carboxamide in some assays (for Compound numbers >370). Apical amiloride is used to inhibit the endogenous ENaC currents while forskolin is applied on both apical and basolateral side to stimulate CFTR. Measurements are done during a 20 minute timeframe with recordings every 2 minutes. The increase in I_{eq} is used as a measure for the increased CFTR activity, EC_{50} values can be generated by measuring impact of different concentrations of compound on I_{eq} on primary cells, for this purpose each transwell is treated with a different compound concentration. Inhibitor-172, an inhibitor specific for CFTR, is used to test the specificity of the tested compounds. Raw data were normalized to percentage activity values using the equation: 100 × (Sample – Negative control)/(Positive control – Negative Control).

Table XXI. Illustrative chronic TECC assay response.

Compound #	%Activity at 1 μM (Ieq*)	EC_{50} (nM) (Ieq*)	%Activity at 1 μM (AUC**)	%Activity at 3 μM (AUC**)	EC_{50} (nM) (AUC**)
30	450	<30			
34	270	<30			
63	325	40			
71	270	19.5			
74	240	<30			
75	316	30			
80	250	19.3			
85	120	>1000			
86	210	30			
87	150	<30			
91	250	<30			
93	220	<30			
95	180	10			
96	310	<30			
104	720	<30			
110	170	<30			
113	310	32			
117	81	>1000			
119	157	>1000			
121	206	74			
128	235	<30			
136			233.2		23.5
142			250		<300
144	350	12			
146	310	30			
150		100			

Compound #	%Activity at 1 μM (Ieq*)	EC_{50} (nM) (Ieq*)	%Activity at 1 μM (AUC**)	%Activity at 3 μM (AUC**)	EC_{50} (nM) (AUC**)
152			482.77		16
155			200		4
158			370.9		
160			190		160
167			260		32
168			282.45		38.2
169			210		2.1
177			419.90		>100
185			453		45.4
187			180		>1000
188			257.3		
190			269		51
193			317.57		
198			477.39		
199			627.48		>1000
200			364.3		
201			250		<300
207			441.31		
215			320		45
219			298.20		
221			245.9		40
226			530		56
228			240		32
229			430		20
230			265.44		27
236			434.22		80

Compound #	%Activity at 1 μM (Ieq*)	EC_{50} (nM) (Ieq*)	%Activity at 1 μM (AUC**)	%Activity at 3 μM (AUC**)	EC_{50} (nM) (AUC**)
238			521.96		
240			288.71		140
241			400		<10
242			308.45		14
243			165.81		
244			238.89		
245			628.25		
246			301.36		61
247			422.93		81
248			275.96		
249			271.29		
250			331.21		
251			336.34		
252			248.51		
263			399.85		77
267					130
269			172.35		
270			250		297
272			285.35		
273			197.06		
274			224.99		>300
279					109
291			255.92		
294					21
297			470.97		≤30
298			318059		

Compound #	%Activity at 1 μM (Ieq*)	EC_{50} (nM) (Ieq*)	%Activity at 1 μM (AUC**)	%Activity at 3 μM (AUC**)	EC_{50} (nM) (AUC**)
304			194.54		
316			452.88		45
317			311.08		24
318			439.94		
320			215.3		
322			440.86		
323			217.91		
325			317.57		
328			531.7	423.1	96
331			537.3		10
334				345.13	100
337			299.50		
340			216.53		
348			343.24		200
365				521.8	200
366			427.95		
369			583.16		8.3
370				226.54	
379			370		43
380				250	
381				441	4105
382		204.7		347	100
383				299	2
385					12.3
396				259.4666	
397				251.7766	

Compound #	%Activity at 1 μM (Ieq*)	EC_{50} (nM) (Ieq*)	%Activity at 1 μM (AUC**)	%Activity at 3 μM (AUC**)	EC_{50} (nM) (AUC**)
399			244.7508		
400			230		
402			345.045		12.1
404			433.3333		
405			323.3333		
406			235		
407			310		48.94
408			430		21
409			420		149.8
410			233.3333		1.582
415			196.1812		28.4
416			288.6036		118.9
417			256.6667		
418			196.6667		19.19
420			223.3333		0
421			193.3333		45.63
422			320		
423			365		39.83
424				462.0976	
429			180		83.75
431			280		
440			696.6667		2.98
441			236.6667		205.8
445			406.6667		
447			330		
448			116.8948		

Compound #	%Activity at 1 μM (Ieq*)	EC_{50} (nM) (Ieq*)	%Activity at 1 μM (AUC**)	%Activity at 3 μM (AUC**)	EC_{50} (nM) (AUC**)
456			261.1621		
469			293.3333		108.2
470			210		
471			296.6667		
472			181.0865		34.24
473			243.3333		
474			226.6667		
480			548.575		
484			380		
487			340		
493			271.4141		370.8
495				262.4635	
517				309.141	
522			666.6667		21.95
523				460.2177	
525			477.2665		50.35
526			400		14.23
527			370.693		
529			520		19.11
530			326.6667		
535			335.0294		
537				261.5724	
541			320		
546				282.0317	
549			373.3333		242.7
551			239.0643		

Compound #	%Activity at 1 μM (Ieq*)	EC_{50} (nM) (Ieq*)	%Activity at 1 μM (AUC**)	%Activity at 3 μM (AUC**)	EC_{50} (nM) (AUC**)
552			235.2857		
555			296.6667		107
558			221.9818		4.74
559			231.6378		
561			620		
562			289.8854		
569			1156.667		
570				377.5594	
575			246.6667		
576				225.798	
578			936.6667		
583			613.3333		51.3
589			236.6667		
590				220.4586	
594				320	
597			263.3333		
599			116.6667		
605			726.6667		
608				442.1916	
609				306.6667	
611				176.7495	
614				407.7118	
621				256.6667	
623				433.3333	
624				310	
625			403.3333		

Compound #	%Activity at 1 μM (Ieq*)	EC_{50} (nM) (Ieq*)	%Activity at 1 μM (AUC**)	%Activity at 3 μM (AUC**)	EC_{50} (nM) (AUC**)
626				387.4854	
627				446.6667	
628				473.0586	88.4
629				153.3918	6.848
630			125.1944		47.07
631			156.9645		
632				237.1158	29.28
633					204.5
634					137.5
638				341.3493	11.24
645				246.4648	
646				276.7167	23.45
647				420.0246	150.7
648			366.0679		
649				224.5026	
654			293.3333		
656				197.5908	
657				357.6409	
658				260.3278	
659				251.6549	

*Ieq refers to calculations based on the maximum current.

**AUC is the full area under the curve upon forskolin stimulation.

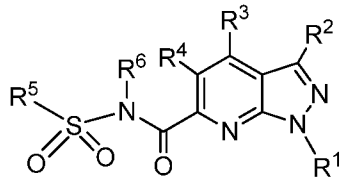
[00810] Information on protein binding of compounds can be retrieved from incubation of compounds in the presence of 40% human serum. For this purpose the differentiated cells are treated basolaterally with test compounds in medium containing 40% human serum (Sigma; H4522) for 24 hours. For electrophysiological recording, the human airway epithelia are

mounted in the TECC heating plate and kept at 37 °C. The epithelia are bathed in a NaCl-Ringer solution (120 mM NaCl, 25 mM $NaHCO_3$, 1.2 mM $CaCl_2$, 1.2 mM $MgCl_2$, 0.8 mM KH_2PO_4, 0.8 mM K_2HPO_4, pH 7.4, 5 mM glucose) on both the basolateral and apical sides. Test compounds (corrector, co-corrector, 4-[(2*R*,4*R*)-4-({[1-(2,2-difluoro-1,3-benzodioxol-5-yl)cyclopropyl]carbonyl}amino)-7-(difluoromethoxy)-3,4-dihydro-2*H*-chromen-2-yl]benzoic acid, and potentiator, *N*-(3-carbamoyl-5,5,7,7-tetramethyl-4,7-dihydro-5*H*-thieno[2,3-*c*]pyran-2-yl)-1*H*-pyrazole-5-carboxamide), are re-added to the recording solution prior to measurement. Apical amiloride is used to inhibit the endogenous ENaC currents while forskolin is applied on both apical and basolateral side to stimulate CFTR. Measurements are done during a 20 minute timeframe with recordings every 2 minutes. The increase in I_{eq} is used as a measure for the increased CFTR activity, EC_{50} values can be generated by measuring impact of different concentrations of compound on I_{eq} on primary cells, for this purpose each transwell is treated with a different compound concentration. Inh-172, an inhibitor specific for CFTR, is used to test the specificity of the tested compounds.

[00811] It is understood that the foregoing detailed description and accompanying examples are merely illustrative and are not to be taken as limitations upon the scope of the invention, which is defined solely by the appended claims and their equivalents. Various changes and modifications to the described embodiments will be apparent to those skilled in the art. Such changes and modifications, including without limitation those relating to the chemical structures, substituents, derivatives, intermediates, syntheses, formulations, or methods, or any combination of such changes and modifications of use of the invention, may be made without departing from the spirit and scope thereof.

We claim:

1. A compound of formula (I) or a pharmaceutically acceptable salt thereof,



(I)

wherein

R^1 is G^{1A}, C_1-C_6 haloalkyl, or C_1-C_6 alkyl; wherein the C_1-C_6 haloalkyl and the C_1-C_6 alkyl are each optionally substituted with one G^{1A};

G^{1A}, at each occurrence, is independently phenyl, 5-6 membered monocyclic heteroaryl, 4-7 membered monocyclic heterocycle, 5-11 membered fused bicyclic heterocycle, or C_3-C_6 monocyclic cycloalkyl; wherein each G^{1A} is optionally substituted with 1, 2, 3, or 4 substituents independently selected from the group consisting of R^{1a} and G^{1B};

G^{1B}, at each occurrence, is independently 4-7 membered monocyclic heterocycle which is optionally substituted with 1, 2, 3, or 4 independently selected R^{1b} groups;

R^2 is hydrogen, C_2-C_4 alkenyl, C_1-C_6 alkyl, C_1-C_6 haloalkyl, $-OR^{2xa}$, $-N(R^{2xa})(R^{2xb})$, or G^{2A};

R^{2xa}, at each occurrence, is independently C_1-C_6 alkyl, C_1-C_6 haloalkyl, or G^{2B};

R^{2xb} is hydrogen, C_1-C_3 alkyl, or C_1-C_3 haloalkyl;

G^{2A} and G^{2B} are each independently a 4-7 membered monocyclic heterocycle or a C_3-C_6 monocyclic cycloalkyl; wherein G^{2A} and G^{2B} are each optionally substituted with 1, 2, or 3 independently selected R^{2a} groups;

R^3 is G^{3A}, $-G^{3B}$-L^1-G^{3C}, $-G^{3B}$-L^3-G^{3C}-G^{3E}, -(C_1-C_6 alkylenyl)-G^{3D}, $-OR^{3a}$, or $-N(R^{3a})(R^{3b})$;

R^{3a}, at each occurrence, is independently G^{3D}, C_1-C_6 haloalkyl, or C_1-C_6 alkyl; wherein the C_1-C_6 haloalkyl and the C_1-C_6 alkyl are each optionally substituted with one or two substituents independently selected from the group consisting of G^{3D}, $-OR^{3xa}$, and $-N(R^{3xb})_2$;

R^{3xa} and R^{3xb}, at each occurrence, are each independently hydrogen, C_1-C_6 haloalkyl, C_1-C_6 alkyl, or G^{3D};

R^{3b} is hydrogen, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

L^1 is a bond, C_1-C_6 alkylenyl, $(C_1$-C_6 alkylenyl$)_r$-L^2-$(C_1$-C_6 alkylenyl$)_s$, or O-$(C_1$-C_6 alkylenyl)-C(O), wherein the left end of the L^1 moiety is attached to G^{3B};

L^2 is O, $N(R^x)$, C(O), $N(R^x)C(O)$, or $C(O)N(R^x)$; wherein each R^x is independently hydrogen, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

L^3 is a bond or C_1-C_6 alkylenyl;

r is 0 or 1;

s is 0 or 1;

G^{3A}, G^{3B}, and G^{3C} and each independently C_3-C_{11} cycloalkyl, phenyl, 5-6 membered monocyclic heteroaryl, or 4-11 membered heterocycle; wherein G^{3A}, G^{3B}, and G^{3C} are each optionally substituted with 1, 2, 3, or 4 independently selected R^e groups;

G^{3D}, at each occurrence, is independently C_3-C_8 monocyclic cycloalkyl, 4-7 membered monocyclic heterocycle, a 5-11 membered fused bicyclic heterocycle, or a 5-11 membered spiro heterocycle; wherein each G^{3D} is optionally substituted with 1, 2, 3, or 4 substituents independently selected from the group consisting of R^e and G^{3E};

G^{3E}, at each occurrence, is independently C_3-C_8 monocyclic cycloalkyl or 4-7 membered monocyclic heterocycle; wherein each G^{3E} is optionally substituted with 1, 2, 3, or 4 independently selected R^e groups;

R^4 is hydrogen, C_1-C_3 alkyl, or C_1-C_3 haloalkyl;

R^5 is C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, $-N(R^{5ax})(R^{5bx})$, $-OR^{5dx}$, or G^{5A}; wherein the C_1-C_6 alkyl and the C_1-C_6 haloalkyl are each optionally substituted with one or two substituents independently selected from the group consisting of G^{5A}, -CN, $-N_3$, $-OR^{5ax}$, $-S(O)_2R^{5ax}$, $-S(O)_2N(R^{5ax})(R^{5bx})$, $-N(R^{5ax})(R^{5bx})$, $-N(R^{5bx})S(O)_2R^{5cx}$, $-N(R^{5bx})C(O)R^{5cx}$, $-N(R^{5bx})C(O)N(R^{5ax})(R^{5bx})$, $-N(R^{5bx})C(O)OR^{5cx}$, $-C(O)R^{5ax}$, $-C(O)OR^{5ax}$, $-C(O)N(R^{5bx})S(O)_2R^{5cx}$, and $-C(O)N(R^{5ax})(R^{5bx})$;

R^{5ax} and R^{5bx}, at each occurrence, are each independently hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, $-OR^{5ex}$, $-(C_1$-C_6 alkylenyl)-OR^{5ex}, G^{5A}, or $-(C_1$-C_6 alkylenyl)-G^{5A};

R^{5cx}, at each occurrence, is independently C_1-C_6 alkyl, C_1-C_6 haloalkyl, G^{5A}, or $-(C_1$-C_6 alkylenyl)-G^{5A};

R^{5dx} is C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

R^{5ex} is hydrogen, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

G^{5A}, at each occurrence, is independently C_3-C_{11} cycloalkyl, phenyl, 5-6 membered monocyclic heteroaryl, or 4-11 membered heterocycle; wherein each G^{5A} is optionally substituted with 1, 2, 3, or 4 independently selected R^{5a} groups;

R^{5a}, at each occurrence, is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, C_1-C_6 haloalkyl, oxo, G^{5B}, -CN, NO_2, $-OR^b$, $-OC(O)R^c$, $-OC(O)N(R^d)_2$, $-SR^b$, $-S(O)_2R^b$, $-S(O)_2N(R^d)_2$, $-C(O)R^b$, $-C(O)OR^b$, $-C(O)N(R^d)_2$, $-C(O)N(R^d)S(O)_2R^c$, $-N(R^d)_2$, $-N(R^d)C(O)R^c$, $-N(R^d)S(O)_2R^c$, $-N(R^d)C(O)O(R^b)$, $-N(R^d)C(O)N(R^d)_2$, $-N(R^d)S(O)_2N(R^d)_2$, -(C_1-C_6 alkylenyl)-CN, -(C_1-C_6 alkylenyl)-G^{5B}, -(C_1-C_6 alkylenyl)-OR^b, -(C_1-C_6 alkylenyl)-$OC(O)R^c$, -(C_1-C_6 alkylenyl)-$OC(O)N(R^d)_2$, -(C_1-C_6 alkylenyl)-SR^b, -(C_1-C_6 alkylenyl)-$S(O)_2R^b$, -(C_1-C_6 alkylenyl)-$S(O)_2N(R^d)_2$, -(C_1-C_6 alkylenyl)-$C(O)R^b$, -(C_1-C_6 alkylenyl)-$C(O)OR^b$, -(C_1-C_6 alkylenyl)-$C(O)N(R^d)_2$, -(C_1-C_6 alkylenyl)-$C(O)N(R^d)S(O)_2R^c$, -(C_1-C_6 alkylenyl)-$N(R^d)_2$, -(C_1-C_6 alkylenyl)-$N(R^d)C(O)R^c$, -(C_1-C_6 alkylenyl)-$N(R^d)S(O)_2R^c$, -(C_1-C_6 alkylenyl)-$N(R^d)C(O)O(R^c)$, -(C_1-C_6 alkylenyl)-$N(R^d)C(O)N(R^d)_2$, or -(C_1-C_6 alkylenyl)-$N(R^d)S(O)_2N(R^d)_2$;

R^b and R^d, at each occurrence, are each independently hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, alkoxyalkyl, G^{5B}, or -(C_1-C_6 alkylenyl)-G^{5B};

R^c, at each occurrence, is independently C_1-C_6 alkyl, C_1-C_6 haloalkyl, alkoxyalkyl, G^{5B}, or -(C_1-C_6 alkylenyl)-G^{5B};

G^{5B}, at each occurrence, is independently C_3-C_6 monocyclic cycloalkyl, phenyl, 5-6 membered monocyclic heteroaryl, or 4-7 membered monocyclic heterocycle; wherein each G^{5B} is optionally substituted with 1, 2, 3, or 4 independently selected R^{5b} groups;

R^e, at each occurrence, is independently C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 alkyl, C_1-C_6 haloalkyl, halogen, oxo, -CN, $-N_3$, $-NO_2$, $-OR^f$, $-OC(O)R^g$, $-OC(O)NR^fR^h$, $-SR^f$, $-S(O)_2R^f$, $-S(O)_2NR^fR^h$, $-C(O)R^f$, $-C(O)OR^f$, $-C(O)NR^fR^h$, $-C(O)N(R^h)S(O)_2R^f$, $-N(R^f)_2$, $-N(R^h)C(O)R^h$, $-N(R^h)S(O)_2R^g$, $-N(R^h)C(O)O(R^g)$, $-N(R^h)C(O)NR^fR^h$, or $-N(R^h)S(O)_2NR^fR^h$; wherein the C_1-C_6 haloalkyl and the C_1-C_6 alkyl are each optionally substituted with 1 or 2 substituents independently selected from the

group consisting of -CN, NO_2, $-OR^f$, $-OC(O)R^g$, $-OC(O)NR^fR^h$, $-SR^f$, $-S(O)_2R^f$, $-S(O)_2NR^fR^h$, $-C(O)R^f$, $-C(O)OR^f$, $-C(O)NR^fR^h$, $-C(O)N(R^h)S(O)_2R^f$, $-N(R^f)_2$, $-N(R^h)C(O)R^g$, $-N(R^h)S(O)_2R^g$, $-N(R^h)C(O)O(R^g)$, $-N(R^h)C(O)NR^fR^h$, and $-N(R^h)S(O)_2NR^fR^h$;

R^f, at each occurrence, is independently hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, -(C_1-C_6 alkylenyl)-CN, -(C_1-C_6 alkylenyl)-OR^m, -(C_1-C_6 alkylenyl)-$OC(O)R^n$, -(C_1-C_6 alkylenyl)-$OC(O)N(R^m)_2$, -(C_1-C_6 alkylenyl)-SR^m, -(C_1-C_6 alkylenyl)-$S(O)_2R^m$, -(C_1-C_6 alkylenyl)-$S(O)_2N(R^m)_2$, -(C_1-C_6 alkylenyl)-$C(O)R^m$, -(C_1-C_6 alkylenyl)-$C(O)OR^m$, -(C_1-C_6 alkylenyl)-$C(O)N(R^m)_2$, -(C_1-C_6 alkylenyl)-$C(O)N(R^m)S(O)_2R^n$, -(C_1-C_6 alkylenyl)-$N(R^m)_2$, -(C_1-C_6 alkylenyl)-$N(R^m)C(O)R^n$, -(C_1-C_6 alkylenyl)-$N(R^m)S(O)_2R^n$, -(C_1-C_6 alkylenyl)-$N(R^m)C(O)O(R^n)$, -(C_1-C_6 alkylenyl)-$N(R^m)C(O)N(R^m)_2$, or -(C_1-C_6 alkylenyl)-$N(R^m)S(O)_2N(R^m)_2$

R^g, at each occurrence, is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, -(C_1-C_6 alkylenyl)-CN, -(C_1-C_6 alkylenyl)-OR^m, -(C_1-C_6 alkylenyl)-$OC(O)R^n$, -(C_1-C_6 alkylenyl)-$OC(O)N(R^m)_2$, -(C_1-C_6 alkylenyl)-SR^m, -(C_1-C_6 alkylenyl)-$S(O)_2R^m$, -(C_1-C_6 alkylenyl)-$S(O)_2N(R^m)_2$, -(C_1-C_6 alkylenyl)-$C(O)R^m$, -(C_1-C_6 alkylenyl)-$C(O)OR^m$, -(C_1-C_6 alkylenyl)-$C(O)N(R^m)_2$, -(C_1-C_6 alkylenyl)-$C(O)N(R^m)S(O)_2R^n$, -(C_1-C_6 alkylenyl)-$N(R^m)_2$, -(C_1-C_6 alkylenyl)-$N(R^m)C(O)R^n$, -(C_1-C_6 alkylenyl)-$N(R^m)S(O)_2R^n$, -(C_1-C_6 alkylenyl)-$N(R^m)C(O)O(R^n)$, -(C_1-C_6 alkylenyl)-$N(R^m)C(O)N(R^m)_2$, or -(C_1-C_6 alkylenyl)-$N(R^m)S(O)_2N(R^m)_2$;

R^h, at each occurrence, is independently hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, or -(C_1-C_6 alkylenyl)-OR^m;

R^{1a}, R^{1b}, R^{2a}, and R^{5b}, at each occurrence, are each independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, C_1-C_6 haloalkyl, oxo, -CN, NO_2, $-OR^m$, $-OC(O)R^n$, $-OC(O)N(R^m)_2$, $-SR^m$, $-S(O)_2R^m$, $-S(O)_2N(R^m)_2$, $-C(O)R^m$, $-C(O)OR^m$, -C(O)O(benzyl), $-C(O)N(R^m)_2$, $-C(O)N(R^m)S(O)_2R^n$, $-N(R^m)_2$, $-N(R^m)$(alkoxyalkyl), -N(alkoxyalkyl)$_2$, $-N(R^m)C(O)R^n$, $-N(R^m)S(O)_2R^n$, $-N(R^m)C(O)O(R^n)$, $-N(R^m)C(O)N(R^m)_2$, $-N(R^m)S(O)_2N(R^m)_2$, -(C_1-C_6 alkylenyl)-CN, -(C_1-C_6 alkylenyl)-OR^m, -(C_1-C_6 alkylenyl)-$OC(O)R^n$, -(C_1-C_6 alkylenyl)-$OC(O)N(R^m)_2$, -(C_1-C_6 alkylenyl)-SR^m, -(C_1-C_6 alkylenyl)-$S(O)_2R^m$, -(C_1-C_6

alkylenyl)-$S(O)_2N(R^m)_2$, -(C_1-C_6 alkylenyl)-$C(O)R^m$, -(C_1-C_6 alkylenyl)-$C(O)OR^m$, -(C_1-C_6 alkylenyl)-$C(O)N(R^m)_2$, -(C_1-C_6 alkylenyl)-$C(O)N(R^m)S(O)_2R^n$, -(C_1-C_6 alkylenyl)-$N(R^m)_2$, -(C_1-C_6 alkylenyl)-$N(R^m)C(O)R^n$, -(C_1-C_6 alkylenyl)-$N(R^m)S(O)_2R^n$, -(C_1-C_6 alkylenyl)-$N(R^m)C(O)O(R^n)$, -(C_1-C_6 alkylenyl)-$N(R^m)C(O)N(R^n)_2$, or -(C_1-C_6 alkylenyl)-$N(R^m)S(O)_2N(R^n)_2$;

R^m, at each occurrence, is independently hydrogen, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

R^n, at each occurrence, is independently C_1-C_6 alkyl or C_1-C_6 haloalkyl;

R^6 is hydrogen, C_1-C_6 alkyl, or C_1-C_6 haloalkyl; or

R^5 and R^6 together form a C_1-C_6 alkylenyl or -$N(R^z)$-(C_1-C_6 alkylenyl)- wherein the $N(R^z)$ is attached to the $S(O)_2$ moiety of formula (I); and

R^z is hydrogen, C_1-C_6 alkyl, or C_1-C_6 haloalkyl.

2. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein R^1 is G^{1A}, C_1-C_6 haloalkyl, or C_1-C_6 alkyl.

3. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein R^1 is G^{1A}.

4. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein R^1 is G^{1A}; wherein G^{1A} is optionally substituted phenyl or optionally substituted 5-6 membered monocyclic heteroaryl.

5. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein R^2 is C_1-C_6 alkyl, C_1-C_6 haloalkyl, -OR^{2xa}, or G^{2A}.

6. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein R^2 is C_1-C_6 alkyl, C_1-C_6 haloalkyl, or G^{2A}; and

G^{2A} is an optionally substituted C_3-C_6 monocyclic cycloalkyl.

7. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein R^2 is -OR^{2xa}.

8. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein R^3 is G^{3A}, $-G^{3B}-L^1-G^{3C}$, or $-OR^{3a}$.

9. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein R^3 is G^{3A} or $-G^{3B}-L^1-G^{3C}$.

10. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein R^3 is G^{3A}; and

G^{3A} is optionally substituted phenyl, optionally substituted 5-6 membered monocyclic heteroaryl, or optionally substituted 4-11 membered heterocycle.

11. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein R^3 is $-G^{3B}-L^1-G^{3C}$;

G^{3B} is phenyl, 5-6 membered monocyclic heteroaryl, or 4-7 membered monocyclic heterocycle; each of which is optionally substituted; and

G^{3C} is C_3-C_6 monocyclic cycloalkyl, phenyl, 5-6 membered monocyclic heteroaryl, or 4-7 membered monocyclic heterocycle; each of which is optionally substituted.

12. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein R^3 is $-OR^{3a}$; and

R^{3a} is G^{3D}, C_1-C_6 haloalkyl, or C_1-C_6 alkyl; wherein the C_1-C_6 haloalkyl and the C_1-C_6 alkyl are each substituted with one or two substituents independently selected from the group consisting of G^{3D}, $-OR^{3xa}$, and $-N(R^{3xb})_2$.

13. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein R^5 is C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, or C_1-C_6 haloalkyl; wherein the C_1-C_6 alkyl and the C_1-C_6 haloalkyl are each optionally substituted with one or two substituents independently selected from the group consisting of G^{5A}, -CN, $-N_3$, $-OR^{5ax}$, $-S(O)_2R^{5ax}$, $-S(O)_2N(R^{5ax})(R^{5bx})$, $-N(R^{5ax})(R^{5bx})$, $-N(R^{5bx})S(O)_2R^{5cx}$,

$-N(R^{5bx})C(O)R^{5cx}$, $-N(R^{5bx})C(O)N(R^{5ax})(R^{5bx})$, $-N(R^{5bx})C(O)OR^{5cx}$, $-C(O)R^{5ax}$, $-C(O)OR^{5ax}$, $-C(O)N(R^{5bx})S(O)_2R^{5cx}$, and $-C(O)N(R^{5ax})(R^{5bx})$.

14. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein R^5 is $-N(R^{5ax})(R^{5bx})$.

15. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein R^5 is G^{5A}.

16. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein
R^1 is G^{1A}, C_1-C_6 haloalkyl, or C_1-C_6 alkyl; and
R^2 is C_1-C_6 alkyl, C_1-C_6 haloalkyl, or G^{2A}.

17. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein
R^1 is G^{1A};
R^2 is C_1-C_6 alkyl or G^{2A}; and
R^3 is G^{3A}, $-G^{3B}$-L^1-G^{3C}, or $-OR^{3a}$.

18. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein
R^1 is G^{1A};
R^2 is C_1-C_6 alkyl or G^{2A}; and
R^5 is C_1-C_6 alkyl or C_1-C_6 haloalkyl.

19. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein
R^1 is G^{1A};
R^2 is C_1-C_6 alkyl or G^{2A}; and
R^5 is C_1-C_6 alkyl which is substituted with one substituent selected from the group consisting of G^{5A}, -CN, $-N_3$, $-OR^{5ax}$, $-N(R^{5ax})(R^{5bx})$, $-N(R^{5bx})C(O)R^{5cx}$, $-N(R^{5bx})C(O)OR^{5cx}$, $-C(O)OR^{5ax}$, and $-C(O)N(R^{5ax})(R^{5bx})$.

20. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein

R^1 is G^{1A};

R^2 is C_1-C_6 alkyl or G^{2A}; and

R^5 is -$N(R^{5ax})(R^{5bx})$.

21. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein

R^1 is G^{1A};

R^2 is C_1-C_6 alkyl or G^{2A}; and

R^5 is G^{5A}.

22. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein

R^1 is G^{1A}; wherein G^{1A} is optionally substituted phenyl, or optionally substituted 5-6 membered monocyclic heteroaryl;

R^2 is C_1-C_6 alkyl or G^{2A}; wherein G^{2A} is an optionally substituted C_3-C_6 monocyclic cycloalkyl;

R^3 is G^{3A}, -G^{3B}-L^1-G^{3C}, or –OR^{3a}; and

R^5 is C_1-C_6 alkyl which is substituted with one substituent selected from the group consisting of G^{5A}, -CN, -N_3, -OR^{5ax}, -$N(R^{5ax})(R^{5bx})$, -$N(R^{5bx})C(O)R^{5cx}$, -$N(R^{5bx})C(O)OR^{5cx}$, -$C(O)OR^{5ax}$, and -$C(O)N(R^{5ax})(R^{5bx})$.

23. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein

R^1 is G^{1A}; wherein G^{1A} is optionally substituted phenyl or optionally substituted 5-6 membered monocyclic heteroaryl;

R^2 is C_1-C_6 alkyl or G^{2A}; wherein G^{2A} is an optionally substituted C_3-C_6 monocyclic cycloalkyl;

R^3 is G^{3A}, -G^{3B}-L^1-G^{3C}, or –OR^{3a}; and

R^5 is C_1-C_6 alkyl or C_1-C_6 haloalkyl.

24. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein

R^1 is G^{1A}; wherein G^{1A} is optionally substituted phenyl or optionally substituted 5-6 membered monocyclic heteroaryl;

R^2 is C_1-C_6 alkyl, or G^{2A}; wherein G^{2A} is an optionally substituted C_3-C_6 monocyclic cycloalkyl;

R^3 is G^{3A}, -G^{3B}-L^1-G^{3C}, or –OR^{3a}; and

R^5 is -$N(R^{5ax})(R^{5bx})$ or -OR^{5dx}.

25. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein

R^1 is G^{1A}; wherein G^{1A} is optionally substituted phenyl or optionally substituted 5-6 membered monocyclic heteroaryl;

R^2 is C_1-C_6 alkyl, or G^{2A}; wherein G^{2A} is an optionally substituted C_3-C_6 monocyclic cycloalkyl;

R^3 is G^{3A}, -G^{3B}-L^1-G^{3C}, or –OR^{3a}; and

R^5 is G^{5A}.

26. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein

R^3 is -G^{3B}-L^3-G^{3C}-G^{3E};

G^{3B} is phenyl, 5-6 membered heteroaryl, or 4-11 membered heterocycle; each of which is optionally substituted;

G^{3C} is optionally substituted 4-11 membered heterocycle; and

G^{3E} is optionally substituted C_3-C_8 monocyclic cycloalkyl.

27. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein

R^1 is G^{1A}; wherein G^{1A} is phenyl, 5-6 membered monocyclic heteroaryl, or C_3-C_6 monocyclic cycloalkyl; each of which is optionally substituted;

R^2 is C_1-C_6 alkyl, -OR^{2xa}, or G^{2A}; wherein G^{2A} is an optionally substituted C_3-C_6 monocyclic cycloalkyl; and

R^3 is G^{3A}, -G^{3B}-L^1-G^{3C}, -G^{3B}-L^3-G^{3C}- G^{3E}, -(C_1-C_6 alkylenyl)-G^{3D}, or –OR^{3a}.

28. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein

R^1 is G^{1A}; wherein G^{1A} is phenyl, 5-6 membered monocyclic heteroaryl, or C_3-C_6 monocyclic cycloalkyl; each of which is optionally substituted;

R^2 is C_1-C_6 alkyl, -OR^{2xa}, or G^{2A}; wherein G^{2A} is an optionally substituted C_3-C_6 monocyclic cycloalkyl;

R^3 is G^{3A}, -G^{3B}-L^1-G^{3C}, -G^{3B}-L^3-G^{3C}- G^{3E}, -(C_1-C_6 alkylenyl)-G^{3D}, or –OR^{3a}; and

R^5 is C_1-C_6 alkyl or C_1-C_6 haloalkyl.

29. The compound of any one of claims 1- 28 or a pharmaceutically acceptable salt thereof, wherein

R^6 is hydrogen.

30. The compound of any one of claims 1 - 28 or a pharmaceutically acceptable salt thereof, wherein

R^6 is C_1-C_6 alkyl or C_1-C_6 haloalkyl.

31. The compound of any one of claims 1-12, 16, 17, and 27 or a pharmaceutically acceptable salt thereof, wherein

R^5 and R^6 together form a C_1-C_6 alkylenyl a -$N(R^z)$-(C_1-C_6 alkylenyl)- wherein the $N(R^z)$ is attached to the $S(O)_2$ moiety of formula (I).

32. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein the compound is selected from the group consisting of:

N-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(benzenesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-methyl-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-*N*-(trifluoromethanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(cyclopropanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1-[3-(trifluoromethoxy)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-1-phenyl-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-[2-(dimethylamino)pyrimidin-5-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(azetidin-1-yl)phenyl]-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-[2-(morpholin-4-yl)pyrimidin-5-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-*tert*-butyl-1-cyclopentyl-*N*-(methanesulfonyl)-4-[6-(morpholin-4-yl)pyridin-3-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-3-methyl-1-phenyl-4-(piperidin-1-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-(4-methoxyphenyl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-4-(4-methoxyphenyl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1-[3-(pyrrolidin-1-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-1-(6-methoxypyridin-3-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(3-chloro-4-methylphenyl)-*N*-(methanesulfonyl)-4-(4-methoxyphenyl)-3-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-3-methyl-1-phenyl-4-(piperidin-1-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[2-(morpholin-4-yl)pyrimidin-5-yl]-1-phenyl-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(2,4-difluorophenyl)-*N*-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-[6-(dimethylamino)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(3,5-difluorophenyl)-*N*-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(3,5-dimethylphenyl)-*N*-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(3,4-difluorophenyl)-*N*-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-3-methyl-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-(4-methoxyphenyl)-3-methyl-1-(3-methylphenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-4-(4-methoxyphenyl)-3-methyl-1-(3-methylphenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[2-(dimethylamino)pyrimidin-5-yl]-*N*-(methanesulfonyl)-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[2-(dimethylamino)pyrimidin-5-yl]-*N*-(ethanesulfonyl)-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(dimethylamino)pyridin-3-yl]-*N*-(methanesulfonyl)-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(dimethylamino)pyridin-3-yl]-*N*-(ethanesulfonyl)-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[6-(morpholin-4-yl)pyridin-3-yl]-1-phenyl-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-4-[6-(morpholin-4-yl)pyridin-3-yl]-1-phenyl-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-1-[3-(3-methoxyazetidin-1-yl)phenyl]-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-3-methyl-4-[6-(morpholin-4-yl)pyridin-3-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4,4-difluorocyclohexyl)-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-(oxan-3-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-(oxan-3-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-{4-[3-(dimethylamino)azetidin-1-yl]phenyl}-*N*-(methanesulfonyl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-{4-[3-(dimethylamino)azetidin-1-yl]phenyl}-*N*-(ethanesulfonyl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(3,3-dimethylazetidin-1-yl)phenyl]-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-[6-(morpholin-4-yl)pyridin-3-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(ethanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(3-fluoropyrrolidin-1-yl)phenyl]-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-3-methyl-4-[6-(morpholin-4-yl)pyridin-3-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(ethanesulfonyl)-3-methyl-4-[6-(morpholin-4-yl)pyridin-3-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-[2-(dimethylamino)pyrimidin-5-yl]-*N*-(methanesulfonyl)-3-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-[2-(dimethylamino)pyrimidin-5-yl]-*N*-(ethanesulfonyl)-3-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-{6-[methyl(oxan-4-yl)amino]pyridin-3-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

methyl 3-{1-cyclohexyl-4-[2-(dimethylamino)pyrimidin-5-yl]-6-[(ethanesulfonyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-3-yl}azetidine-1-carboxylate;

1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-[6-(morpholin-4-yl)pyridin-3-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(dimethylamino)phenyl]-*N*-(ethanesulfonyl)-4-[6-(morpholin-4-yl)pyridin-3-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclopentyl-4-[6-(dimethylamino)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclopentyl-4-[6-(dimethylamino)pyridin-3-yl]-*N*-(ethanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-3-methyl-4-[6-(morpholin-4-yl)pyridin-3-yl]-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-3-methyl-4-[6-(morpholin-4-yl)pyridin-3-yl]-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-[2-(morpholin-4-yl)pyrimidin-5-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(2,4-difluorophenyl)-*N*-(methanesulfonyl)-3-methyl-4-[6-(morpholin-4-yl)pyridin-3-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(2,4-difluorophenyl)-*N*-(ethanesulfonyl)-3-methyl-4-[6-(morpholin-4-yl)pyridin-3-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(dimethylamino)phenyl]-*N*-(ethanesulfonyl)-4-[2-(morpholin-4-yl)pyrimidin-5-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-{6-[(2-methoxyethyl)(methyl)amino]pyridin-3-yl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-[6-(3,3-difluoropyrrolidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(3-chlorophenyl)-*N*-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(3-chlorophenyl)-*N*-(ethanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(3-fluorophenyl)-*N*-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-1-(3-fluorophenyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1-[4-(trifluoromethoxy)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1-[4-(trifluoromethoxy)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-1-(3-methoxyphenyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-1-(3-methoxyphenyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-{6-[methyl(oxan-4-yl)amino]pyridin-3-yl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-{4-[(2-methoxyethyl)(methyl)amino]phenyl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-1-{3-[(2-methoxyethyl)(methyl)amino]phenyl}-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(dimethylamino)phenyl]-4-[2-(dimethylamino)pyrimidin-5-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(dimethylamino)phenyl]-4-[2-(dimethylamino)pyrimidin-5-yl]-*N*-(ethanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(4-acetamidophenyl)-1-cyclohexyl-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(4-cyanopiperidin-1-yl)phenyl]-1-cyclohexyl-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(4-cyanopiperidin-1-yl)phenyl]-1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-{4-[(2-methoxyethyl)(methyl)amino]phenyl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-{6-[(2-methoxyethyl)(methyl)amino]pyridin-3-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-{6-[(2-methoxyethyl)(methyl)amino]pyridin-3-yl}-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-{6-[methyl(oxan-4-yl)amino]pyridin-3-yl}-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-{4-[(2-methoxyethyl)(methyl)amino]phenyl}-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-{6-[methyl(oxan-4-yl)amino]pyridin-3-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(ethanesulfonyl)-4-{6-[methyl(oxan-4-yl)amino]pyridin-3-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-{2-[methyl(oxan-4-yl)amino]pyrimidin-5-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-3-cyclopropyl-4-[6-(dimethylamino)pyridin-3-yl]-*N*-(ethanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-[6-(2,6-dimethylmorpholin-4-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-[6-(2,2-dimethylmorpholin-4-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[2-(4-cyanopiperidin-1-yl)pyrimidin-5-yl]-1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-{4-[methyl(oxan-4-yl)amino]phenyl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-{4-[methyl(oxan-4-yl)amino]phenyl}-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyano-4-methylpiperidin-1-yl)pyridin-3-yl]-1-cyclohexyl-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[2-(4-cyanopiperidin-1-yl)pyrimidin-5-yl]-*N*-(methanesulfonyl)-1-[3-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-{4-[3-(dimethylamino)pyrrolidin-1-yl]phenyl}-*N*-(methanesulfonyl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-1-(3-methylphenyl)-4-(piperidin-1-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-1-(3-methylphenyl)-4-(piperidin-1-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(4-cyanopiperidin-1-yl)phenyl]-3-cyclobutyl-1-cyclohexyl-*N*-(methanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-cyclobutyl-1-cyclohexyl-*N*-(methanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(3-hydroxyazetidin-1-yl)phenyl]-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-[6-(3-methoxypyrrolidin-1-yl)pyridin-3-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

methyl 3-{4-(4-acetamidophenyl)-1-(3,5-difluorophenyl)-6-[(methanesulfonyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-3-yl}azetidine-1-carboxylate;

1-cyclohexyl-4-[6-(3-fluoropiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-{4-[(2-methoxyethyl)(methyl)amino]phenyl}-3-(propan-2-yl)-1-[3-(pyrrolidin-1-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-{4-[methyl(oxan-4-yl)amino]phenyl}-3-(propan-2-yl)-1-[3-(pyrrolidin-1-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-{4-[methyl(oxan-4-yl)amino]phenyl}-1-[3-(pyrrolidin-1-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-4-[2-(morpholin-4-yl)pyrimidin-5-yl]-1-phenyl-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(2,4-difluorophenyl)-*N*-(ethanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(3-chloro-4-methylphenyl)-*N*-(ethanesulfonyl)-4-(4-methoxyphenyl)-3-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(3,5-dimethylphenyl)-*N*-(ethanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(3,4-difluorophenyl)-*N*-(ethanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-(4-methoxypiperidin-1-yl)-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-4-(4-methoxypiperidin-1-yl)-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[2-(4-cyanopiperidin-1-yl)pyrimidin-5-yl]-1-cyclohexyl-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-{2-[(2-methoxyethyl)(methyl)amino]pyrimidin-5-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-{6-[bis(2-methoxyethyl)amino]pyridin-3-yl}-1-cyclohexyl-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-{6-[methyl(oxolan-3-yl)amino]pyridin-3-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-{2-[methyl(oxan-4-yl)amino]pyrimidin-5-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[6-(dimethylamino)pyridin-2-yl]-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1-[3-(trifluoromethoxy)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(3,4-difluorophenyl)-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-[6-(morpholin-4-yl)pyridin-2-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(2,6-difluoro-4-methoxyphenyl)-1-(3-fluoro-5-methoxyphenyl)-*N*-(methanesulfonyl)-3-methyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(4-cyanopiperidin-1-yl)phenyl]-1-(3,5-difluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(4-cyanopiperidin-1-yl)phenyl]-1-(3-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-{4-[(2-methoxyethyl)(methyl)amino]phenyl}-3-(propan-2-yl)-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-{6-[methyl(oxan-4-yl)amino]pyridin-3-yl}-3-(propan-2-yl)-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-{2-[methyl(oxan-4-yl)amino]pyrimidin-5-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(4-cyanopiperidin-1-yl)phenyl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-[2-(morpholin-4-yl)pyridin-4-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-3-(1-methylcyclobutyl)-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-3-(1-methylcyclobutyl)-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[2-(4-cyanopiperidin-1-yl)pyrimidin-5-yl]-1-(2,4-difluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-1-(2,4-difluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(4-cyanopiperidin-1-yl)phenyl]-1-(2,4-difluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-(4-methoxypiperidin-1-yl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(1,1-dioxo-1λ^6-thiolane-3-sulfonyl)-4-(4-methoxypiperidin-1-yl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-1-(oxan-3-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(2-methoxyethanesulfonyl)-4-(4-methoxypiperidin-1-yl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-(4-methoxypiperidin-1-yl)-1-phenyl-*N*-(3,3,3-trifluoropropane-1-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(1,1-difluoro-5-azaspiro[2.4]heptan-5-yl)-*N*-(methanesulfonyl)-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-(4-methoxypiperidin-1-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-4-{4-[(propan-2-yl)oxy]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-4-(4-propoxypiperidin-1-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[3-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-{4-[2-oxo-2-(pyrrolidin-1-yl)ethoxy]piperidin-1-yl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-(4-methoxypiperidin-1-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-(piperidin-1-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1-[2-(pyrrolidin-1-yl)pyridin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-(1-oxa-7-azaspiro[3.5]nonan-7-yl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(4-cyanopiperidin-1-yl)-1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[4-(2-methoxyethyl)piperidin-1-yl]-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-(3-methoxypiperidin-1-yl)-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-4-(3-methoxypiperidin-1-yl)-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(fluoromethyl)piperidin-1-yl]-*N*-(methanesulfonyl)-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[4-(methanesulfonyl)piperidin-1-yl]-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(4-methoxypiperidin-1-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(4-cyanopiperidin-1-yl)phenyl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1-[2-(pyrrolidin-1-yl)pyridin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[(2-methoxyethyl)(methyl)amino]-1-(3-methylphenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-1-(3-methylphenyl)-4-(8-oxa-2-azaspiro[4.5]decan-2-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(4-butoxypiperidin-1-yl)-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(4-methoxy-4-methylpiperidin-1-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

2-[(2-{[3-cyclobutyl-4-(4-methoxypiperidin-1-yl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl]sulfamoyl}ethyl)carbamoyl]benzoic acid;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[4-(2-methylpropoxy)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-(4-methoxypiperidin-1-yl)-1-phenyl-*N*-(2,2,2-trifluoroethanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(1-oxa-7-azaspiro[3.5]nonan-7-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[3-(difluoromethyl)piperidin-1-yl]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(6-oxa-2-azaspiro[3.5]nonan-2-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(1-oxa-8-azaspiro[4.5]decan-8-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-(cyclohexylmethoxy)-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-4-(piperidin-1-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(2-methoxyethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(2-azaspiro[3.4]octan-2-yl)-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(3-azabicyclo[3.1.0]hexan-3-yl)-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-(4-methoxypiperidin-1-yl)-1-[2-(morpholin-4-yl)pyridin-4-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-(4-methoxypiperidin-1-yl)-3-(propan-2-yl)-1-[2-(pyrrolidin-1-yl)pyridin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-cyclobutyl-*N*-(methanesulfonyl)-1-[2-(pyrrolidin-1-yl)pyridin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(methanesulfonyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(4-cyanopiperidin-1-yl)-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(2-azaspiro[3.5]nonan-2-yl)-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[3-(methoxymethyl)azetidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(*cis*-3-methoxycyclobutyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-(3,3-difluorocyclobutyl)-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-(3,3-dimethylcyclobutyl)-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-(3-fluorocyclobutyl)-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[2-(oxan-4-yl)ethoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[(2*S*)-2-fluoro-2-(oxan-4-yl)ethoxy]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-cyclobutyl-*N*-(methanesulfonyl)-1-[2-(morpholin-4-yl)pyridin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-(1,1-difluoro-5-azaspiro[2.4]heptan-5-yl)-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-(5-oxa-2-azaspiro[3.5]nonan-2-yl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-(7-oxa-2-azaspiro[3.5]nonan-2-yl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(5-azaspiro[2.5]octan-5-yl)-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[(2-methoxyethyl)(methyl)amino]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-(4-methoxypiperidin-1-yl)-*N*-(oxane-4-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

benzyl 4-{[3-cyclobutyl-4-(4-methoxypiperidin-1-yl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl]sulfamoyl}piperidine-1-carboxylate;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-(*cis*-3-fluorocyclobutyl)-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-(*trans*-3-fluorocyclobutyl)-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[(*cis*-4-methoxycyclohexyl)oxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[(*trans*-4-methoxycyclohexyl)oxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-{4-[(benzyloxy)methyl]piperidin-1-yl}-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(2-azaspiro[3.3]heptan-2-yl)-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

methyl 5-{3-cyclobutyl-6-[(methanesulfonyl)carbamoyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}octahydro-1*H*-pyrrolo[3,2-*c*]pyridine-1-carboxylate;

4-(1-acetyloctahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl)-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-(4-methoxypiperidin-1-yl)-1-[6-(morpholin-4-yl)pyridin-2-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-{4-[(1*S*)-2-(dimethylamino)-1-fluoroethyl]piperidin-1-yl}-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(fluoromethyl)piperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[4-(2-methoxypropan-2-yl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(3-azaspiro[5.5]undecan-3-yl)-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(3,4-difluorophenyl)-*N*-(ethanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-1-(3-fluorophenyl)-4-{6-[methyl(oxan-4-yl)amino]pyridin-3-yl}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(cyclopropanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(2-methoxyethanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-1-[2-(morpholin-4-yl)pyridin-4-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(cyclopentyloxy)piperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(cyclohexyloxy)piperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(cyclopropylmethoxy)piperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(2-methoxyethanesulfonyl)-4-(4-methoxyphenyl)-3-methyl-1-(2-methylpropyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(2-methoxyethanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-(oxolan-3-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(2-methoxyethanesulfonyl)-4-[4-(morpholin-4-yl)phenyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(2-methoxyethanesulfonyl)-4-(4-methoxyphenyl)-3-methyl-1-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclopropyl-*N*-(2-methoxyethanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(2-methoxyethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[(2*R*)-2-fluoro-2-(oxan-4-yl)ethoxy]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[(3,3-difluorocyclopentyl)methoxy]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(cyclopropanesulfonyl)-3-methyl-4-[4-(morpholin-4-yl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(4-cyanopiperidin-1-yl)-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(1-methoxyethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-4-[4-(1,1,1-trifluoro-2-methoxypropan-2-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[2-(1,1-dioxo-1λ^6,4-thiazinan-4-yl)ethoxy]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(hydroxymethyl)piperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-(1-methyl-1*H*-pyrazole-4-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-{6-[bis(2-methoxyethyl)amino]pyridin-3-yl}-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-methoxy-4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-[2-(morpholin-4-yl)pyridin-4-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(2-methoxyethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-[2-(morpholin-4-yl)pyridin-4-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(1,2-dimethyl-1*H*-imidazole-4-sulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(2-methoxyethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-{6-[bis(2-methoxyethyl)amino]pyridin-3-yl}-*N*-(methanesulfonyl)-1-[2-(morpholin-4-yl)pyridin-4-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-*N*-(1*H*-pyrazole-4-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[(3-methyloxetan-3-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-{4-[(1,1-dioxo-1λ^6,4-thiazinan-4-yl)methyl]-4-methoxypiperidin-1-yl}-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(2-methoxyethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-(*trans*-3-methylcyclobutyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-1-phenyl-3-[(piperidin-4-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

tert-butyl 4-({4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-6-[(methanesulfonyl)carbamoyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-3-yl}oxy)piperidine-1-carboxylate;

3-cyclobutyl-*N*-[2-(1,3-dioxo-1,3-dihydro-2*H*-isoindol-2-yl)ethanesulfonyl]-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(2-aminoethanesulfonyl)-3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(cyclobutylmethyl)-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(cyclobutylmethyl)-*N*-(2-methoxyethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-(2-methylpropyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(2-methoxyethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-(2-methylpropyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-4-[4-(2,2,2-trifluoroethyl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[2-(morpholin-4-yl)ethanesulfonyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-(1-methyl-6-oxo-1,6-dihydropyridazin-3-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(2-methoxyethanesulfonyl)-4-[(3-methyloxetan-3-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-4-[4-(propan-2-yl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(2-methoxyethanesulfonyl)-1-phenyl-4-[4-(propan-2-yl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[3-(morpholin-4-yl)propane-1-sulfonyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-[2-(dimethylamino)ethanesulfonyl]-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[(1-acetyl-4-fluoropiperidin-4-yl)methoxy]-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(2-methoxyethanesulfonyl)-3-[(oxolan-3-yl)oxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(2-methoxyethanesulfonyl)-3-(*trans*-3-methylcyclobutyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-[(oxolan-3-yl)oxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-[3-(dimethylamino)phenyl]-*N*-(methanesulfonyl)-4-[(oxan-4-yl)methoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-[2-(morpholin-4-yl)pyrimidin-4-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(4-cyclobutylpiperazin-1-yl)-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[3-(morpholin-4-yl)propoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[(3,3-difluoro-1-methylcyclobutyl)methoxy]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[(oxolan-2-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[(oxan-4-yl)methoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[2-(oxan-4-yl)ethoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-(1-methyl-1*H*-imidazole-4-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(3,5-dimethyl-1,2-oxazole-4-sulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

methyl 3-({3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)propanoate;

3-({3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)propanoic acid;

N-[3-(dimethylamino)propane-1-sulfonyl]-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-*N*-[3-(pyrrolidin-1-yl)propane-1-sulfonyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[3-(morpholin-4-yl)propoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[(3-methyloxetan-3-yl)methoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(2-methoxypropan-2-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[(oxolan-2-yl)methoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[(1-acetylpiperidin-4-yl)methoxy]-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

methyl 4-[({3-cyclobutyl-6-[(methanesulfonyl)carbamoyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}oxy)methyl]piperidine-1-carboxylate;

3-cyclobutyl-*N*-[3-(dimethylamino)-3-oxopropane-1-sulfonyl]-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[3-(dimethylamino)propoxy]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-*N*-(methanesulfonyl)-3-[(oxetan-3-yl)oxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[(2-methoxyethyl)(methyl)amino]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-[3-(azetidin-1-yl)propane-1-sulfonyl]-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[3-(dimethylamino)propoxy]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-4-[4-(2-hydroxypropan-2-yl)piperidin-1-yl]-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[2-(1-methylpiperidin-2-yl)ethoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[(3,3-difluoro-1-methylcyclobutyl)methoxy]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[3-(piperidin-1-yl)propoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[(1-acetyl-4-fluoropiperidin-4-yl)methoxy]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-{2-[(oxetan-3-yl)(propan-2-yl)amino]ethoxy}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-4-{[4-(propan-2-yl)morpholin-3-yl]methoxy}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[(1,3-dimethoxypropan-2-yl)oxy]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[(1,4-dioxan-2-yl)methoxy]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-{2-[(oxetan-3-yl)oxy]ethoxy}-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-4-[3-(piperidin-1-yl)propoxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(2-methoxyethanesulfonyl)-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(2-hydroxypropan-2-yl)piperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[(oxan-4-yl)methoxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(dimethylamino)piperidin-1-yl]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(1'-methyl[4,4'-*b*ipiperidin]-1-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[(1-acetylpiperidin-4-yl)methoxy]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

methyl 4-({[1-(4-fluorophenyl)-6-[(methanesulfonyl)carbamoyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl]oxy}methyl)piperidine-1-carboxylate;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[2-(1-methylpiperidin-2-yl)ethoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[(1,3-dimethoxypropan-2-yl)oxy]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-{2-[(oxetan-3-yl)(propan-2-yl)amino]ethoxy}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(cyanomethyl)-4-hydroxypiperidin-1-yl]-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(4-azidophenyl)-*N*-(3-azidopropane-1-sulfonyl)-1-[3-(dimethylamino)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-4-[4-(2,2,2-trifluoroethyl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(2-methoxyethanesulfonyl)-1-phenyl-4-[4-(2,2,2-trifluoroethyl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-{4-[2-(morpholin-4-yl)ethyl]piperidin-1-yl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

rac-4-[(3a*R*,7a*S*)-1-acetyloctahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl]-3-cyclobutyl-*N*-[3-(morpholin-4-yl)propane-1-sulfonyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(cyclopropanesulfonyl)-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(ethanesulfonyl)-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(methanesulfonyl)-1-[2-(morpholin-4-yl)pyridin-4-yl]-4-[(oxan-4-yl)methoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

ethyl 4-[1-(4-fluorophenyl)-6-[(methanesulfonyl)carbamoyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl]piperazine-1-carboxylate;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(3-methyl-2-oxo-1-oxa-3,8-diazaspiro[4.5]decan-8-yl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-4-[3-(trifluoromethyl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[4-(2-methoxyethyl)piperazin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(2,4-dioxo-1,3,8-triazaspiro[4.5]decan-8-yl)-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(ethoxymethyl)-4-fluoropiperidin-1-yl]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-{4-fluoro-4-[(2-methoxyethoxy)methyl]piperidin-1-yl}-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[(3*R*,4*R*)-3-fluoro-4-hydroxypiperidin-1-yl]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-fluoro-4-(methoxymethyl)piperidin-1-yl]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-{3-fluoro-3-[(2-methoxyethoxy)methyl]piperidin-1-yl}-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-[3-(morpholin-4-yl)propane-1-sulfonyl]-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-([1,4'-*b*ipiperidin]-1'-yl)-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[(3*R*)-3-(hydroxymethyl)piperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[(3*R*)-3-(hydroxymethyl)piperidin-1-yl]-*N*-[3-(morpholin-4-yl)propane-1-sulfonyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[(oxan-4-yl)methoxy]-1-phenyl-*N*-[4-(pyrrolidin-1-yl)piperidine-1-sulfonyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-[(2*S*)-2-(4-methylpiperazine-1-carbonyl)pyrrolidine-1-sulfonyl]-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-([1,4'-*b*ipiperidine]-1'-sulfonyl)-3-cyclobutyl-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-[methyl(propyl)sulfamoyl]-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-[ethyl(propyl)sulfamoyl]-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

ethyl 4-[({3-cyclobutyl-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)amino]piperidine-1-carboxylate;

N-(4-acetyl-1,4-diazepane-1-sulfonyl)-3-cyclobutyl-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(morpholine-4-sulfonyl)-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-[4-(morpholin-4-yl)piperidine-1-sulfonyl]-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-[4-(4-methylpiperazine-1-carbonyl)piperidine-1-sulfonyl]-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(4-methylpiperazine-1-sulfonyl)-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(2-methylpropane-2-sulfonyl)-4-[(oxan-4-yl)methoxy]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(4-azidophenyl)-*N*-(but-3-yne-1-sulfonyl)-1-[3-(dimethylamino)phenyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(cyanomethanesulfonyl)-3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-([1,4'-*b*ipiperidin]-1'-yl)-3-cyclobutyl-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(2-hydroxyethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(3-hydroxypropane-1-sulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-*N*-(piperidine-4-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-(oxolane-3-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(2,6-dimethylpyridin-4-yl)-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-(1,1-dioxo-1λ^6,4-thiazinan-4-yl)-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-*N*-[2-(1*H*-pyrazol-1-yl)ethanesulfonyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

benzyl [2-({3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)ethyl]carbamate;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-(1-methylcyclopropane-1-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-(2-methylpropane-1-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

methyl ({3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)acetate;

benzyl 3-({3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)pyrrolidine-1-carboxylate;

tert-butyl 4-[1-(4-fluorophenyl)-6-[(methanesulfonyl)carbamoyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl]piperidine-1-carboxylate; and

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[2-(methoxymethyl)morpholin-4-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(morpholine-4-sulfonyl)-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[4-(propan-2-yl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(morpholine-4-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(2-amino-2-oxoethanesulfonyl)-3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-(2-methoxypyridin-4-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(2-acetamidoethanesulfonyl)-3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-*N*-(pyrrolidine-3-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-*N*-[4-(pyrrolidin-1-yl)piperidine-1-sulfonyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[(2*S*)-2-(4-methylpiperazine-1-carbonyl)pyrrolidine-1-sulfonyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-{4-[(2*S*)-2-(methoxymethyl)pyrrolidin-1-yl]piperidine-1-sulfonyl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[methyl(propyl)sulfamoyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-[ethyl(propyl)sulfamoyl]-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

ethyl 4-[({3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)amino]piperidine-1-carboxylate;

N-(4-acetyl-1,4-diazepane-1-sulfonyl)-3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-{4-[(2*R*)-2-(methoxymethyl)pyrrolidin-1-yl]piperidine-1-sulfonyl}-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-(morpholine-4-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[4-(morpholin-4-yl)piperidine-1-sulfonyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[4-(4-methylpiperazine-1-carbonyl)piperidine-1-sulfonyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(4-fluoropiperidine-1-sulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-(4-methylpiperazine-1-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(cyclopropanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(ethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-{4-[(morpholin-4-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(2-methoxyethanesulfonyl)-4-{4-[(morpholin-4-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[(morpholin-4-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(2-methoxyethanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[(morpholin-4-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-{4-[(morpholin-4-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(ethanesulfonyl)-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(cyclopropanesulfonyl)-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(2-methoxyethanesulfonyl)-4-{4-[2-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[2-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-[(1,4-dioxan-2-yl)methanesulfonyl]-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(2-methoxyethanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-[4-(4-methylpiperazine-1-carbonyl)phenyl]-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-[4-(4-methylpiperazine-1-carbonyl)phenyl]-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[(morpholin-4-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[2-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-*N*-(ethanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-*N*-(cyclopropanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-*N*-(oxolane-3-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-(2-methylpyridin-4-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-{4-[2-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-[methyl(propyl)sulfamoyl]-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

ethyl 4-[({3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)amino]piperidine-1-carboxylate;

3-cyclobutyl-*N*-(4-fluoropiperidine-1-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(1-methylcyclopropane-1-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(cyclopropanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(ethanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(2-methoxyethanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-{4-[(2*S*)-2-(methoxymethyl)pyrrolidin-1-yl]piperidine-1-sulfonyl}-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[1-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-{4-[(4-methylpiperazin-1-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[(4-methylpiperazin-1-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[(piperidin-1-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(dimethylsulfamoyl)-3-[(propan-2-yl)oxy]-4-{4-[(pyrrolidin-1-yl)methyl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-{4-[1-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(ethanesulfonyl)-1-(4-fluorophenyl)-4-{4-[1-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(2-methoxyethanesulfonyl)-4-{4-[(morpholin-4-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(2-hydroxyethanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(chloromethanesulfonyl)-3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-1-(4-fluorophenyl)-*N*-(oxolane-3-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[2-(morpholin-4-yl)ethyl]piperidin-1-yl}-*N*-(oxolane-3-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-([1,4'-bipiperidine]-1'-sulfonyl)-3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-*N*-[3-(morpholin-4-yl)propane-1-sulfonyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(4-methylpiperazine-1-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

ethyl 4-{[(3-cyclobutyl-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl)sulfamoyl]amino}piperidine-1-carboxylate;

3-cyclobutyl-*N*-{4-[(2*R*)-2-(methoxymethyl)pyrrolidin-1-yl]piperidine-1-sulfonyl}-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(4-fluoropiperidine-1-sulfonyl)-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(4-methylpiperazine-1-sulfonyl)-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(1-methylcyclopropane-1-sulfonyl)-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(cyclopropanesulfonyl)-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(ethanesulfonyl)-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(2-methoxyethanesulfonyl)-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(2-methylpropane-2-sulfonyl)-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(ethanesulfonyl)-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-(cyclobutyloxy)-1-cyclohexyl-4-{4-[(morpholin-4-yl)methyl]phenyl}-*N*-(oxolane-3-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(oxolane-3-sulfonyl)-4-[4-(pyridin-4-yl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-[4-(pyridin-4-yl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(ethanesulfonyl)-4-[4-(pyridin-4-yl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-[(2-methoxyethyl)(methyl)sulfamoyl]-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-[2-(oxan-4-yl)pyridin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-1-(2-methoxypyridin-4-yl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[(morpholin-4-yl)methyl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[2-(morpholin-4-yl)ethyl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(but-3-yne-1-sulfonyl)-3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-*N*-(ethanesulfonyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[(1*R*)-1-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[(1*S*)-1-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-(cyclobutyloxy)-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[(morpholin-4-yl)methyl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-[methyl(propan-2-yl)sulfamoyl]-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-[ethyl(methyl)sulfamoyl]-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(3-methoxyazetidine-1-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-*N*-(pyrrolidine-1-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-*N*-(2,2,2-trifluoroethanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(morpholine-4-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-([1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-1-(4-fluorophenyl)-*N*-(2-methoxyethanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(dimethylsulfamoyl)-1-[2-(morpholin-4-yl)pyridin-4-yl]-4-[(oxan-4-yl)methoxy]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-[2-(oxan-4-yl)pyridin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(2-hydroxyethanesulfonyl)-4-{4-[2-(morpholin-4-yl)ethyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

methyl 4-(1-{3-cyclobutyl-6-[(dimethylsulfamoyl)carbamoyl]-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperidin-4-yl)piperazine-1-carboxylate;

4-[4-(4-acetylpiperazin-1-yl)piperidin-1-yl]-3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(ethanesulfonyl)-1-(4-fluorophenyl)-4-{4-[(morpholin-4-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[(morpholin-4-yl)methyl]piperidin-1-yl}-*N*-(oxolane-3-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

ethyl 4-[1-(4-fluorophenyl)-6-[(methanesulfonyl)carbamoyl]-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl]piperidine-1-carboxylate;

ethyl 4-{6-[(dimethylsulfamoyl)carbamoyl]-1-(4-fluorophenyl)-3-(propan-2-yl)-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperidine-1-carboxylate;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(3-methylphenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(3-methoxyphenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-[4-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(ethoxymethyl)-4-fluoropiperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-{4-fluoro-4-[(2-methoxyethoxy)methyl]piperidin-1-yl}-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-{3-fluoro-3-[(2-methoxyethoxy)methyl]piperidin-1-yl}-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-fluoro-4-(methoxymethyl)piperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(4-cyanopiperidine-1-sulfonyl)-3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-*N*-(oxetane-3-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(cyclopropanesulfonyl)-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(1-methylcyclopropane-1-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-1-(3-methylphenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-[4-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluoro-3-methylphenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(3-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluoro-3-methylphenyl)-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(3-fluorophenyl)-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[(4-methylpiperazin-1-yl)methyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[(morpholin-4-yl)methyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[(morpholin-4-yl)methyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{[4-(methoxymethyl)piperidin-1-yl]methyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(4-cyano[1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(3-cyanoazetidin-1-yl)piperidin-1-yl]-3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[4-(3-methoxypyrrolidin-1-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-(4-fluoro[1,4'-bipiperidin]-1'-yl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-(4,4-difluoro[1,4'-bipiperidin]-1'-yl)-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(2-cyanomorpholin-4-yl)piperidin-1-yl]-3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[methyl(oxan-4-yl)amino]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-{2-[(propan-2-yl)oxy]pyridin-4-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-{2-[(propan-2-yl)oxy]pyridin-4-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-[2-(oxan-4-yl)pyridin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[4-(2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[3-(morpholin-4-yl)-1-oxa-8-azaspiro[4.5]decan-8-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(dimethylsulfamoyl)-3-[(propan-2-yl)oxy]-4-{4-[4-(propan-2-yl)piperazin-1-yl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-[4-(2-methylpyridin-4-yl)piperazin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-4-[6-(4-cyclopropylpiperazin-1-yl)pyridin-3-yl]-*N*-(dimethylsulfamoyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(3-fluoropyrrolidine-1-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(3-methoxypyrrolidine-1-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[6-(4-cyanopiperidin-1-yl)pyridin-3-yl]-3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-[4-(methoxymethyl)piperidine-1-sulfonyl]-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[4-(3-fluoropyrrolidin-1-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{6-[4-(propan-2-yl)piperazin-1-yl]pyridin-3-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[1-(morpholin-4-yl)ethyl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-{4-[4-(dimethylamino)piperidine-1-carbonyl]phenyl}-*N*-(methanesulfonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-{4-[4-(dimethylamino)piperidine-1-carbonyl]phenyl}-*N*-(2-methoxyethanesulfonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-{4-[4-(dimethylamino)piperidine-1-carbonyl]phenyl}-*N*-(dimethylsulfamoyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[4-(propan-2-yl)piperazin-1-yl]phenyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-*N*-(dimethylsulfamoyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(cyclopropanesulfonyl)-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-[6-(4-methylpiperazin-1-yl)pyridin-3-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{6-[4-(2-methoxyethyl)piperazin-1-yl]pyridin-3-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-4-{4-[4-(propan-2-yl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-*N*-[methyl(propyl)sulfamoyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-*N*-(morpholine-4-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-*N*-(methanesulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-*N*-(1-methylcyclopropane-1-sulfonyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-*N*-(methylsulfamoyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-[4-(4-cyclopropylpiperazin-1-yl)phenyl]-*N*-(dimethylsulfamoyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[3-(trifluoromethyl)pyrrolidin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(3-cyanopyrrolidin-1-yl)piperidin-1-yl]-3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(3-cyano[1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-(3-fluoro[1,4'-bipiperidin]-1'-yl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-{4-[3-(trifluoromethyl)pyrrolidin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(3-cyanopyrrolidin-1-yl)piperidin-1-yl]-3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-(3-cyano[1,4'-bipiperidin]-1'-yl)-3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-(3-fluoro[1,4'-bipiperidin]-1'-yl)-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-*N*-(piperidine-1-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(3-fluoroazetidine-1-sulfonyl)-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[4-(3-methoxyazetidin-1-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[3-(trifluoromethyl)[1,4'-bipiperidin]-1'-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-(3-methoxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(2,2-dimethylmorpholin-4-yl)piperidin-1-yl]-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(2-acetamidoethanesulfonyl)-3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-[2-(difluoromethoxy)pyridin-4-yl]-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(azetidine-1-sulfonyl)-3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-[(2*R*)-2-(methoxymethyl)pyrrolidine-1-sulfonyl]-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-*N*-[(oxan-4-yl)sulfamoyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-[methyl(oxan-4-yl)sulfamoyl]-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(3,3-difluoroazetidine-1-sulfonyl)-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[(3*S*)-4-benzyl-3-methylpiperazin-1-yl]-3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[(3*R*)-4-benzyl-3-methylpiperazin-1-yl]-3-cyclobutyl-1-cyclohexyl-*N*-(dimethylsulfamoyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(4-cyclopropylpiperazin-1-yl)piperidin-1-yl]-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-(9-cyclopropyl-3,9-diazaspiro[5.5]undecan-3-yl)-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[4-(3-methoxyazetidin-1-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[3-(trifluoromethyl)[1,4'-bipiperidin]-1'-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(3-methoxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[4-(2,2-dimethylmorpholin-4-yl)piperidin-1-yl]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

ethyl 4-(1-{3-cyclobutyl-6-[(dimethylsulfamoyl)carbamoyl]-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperidin-4-yl)piperazine-1-carboxylate;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[(2-methoxyethyl)(methyl)amino]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methoxysulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[1-(4,4-difluorocyclohexyl)piperidin-4-yl]-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[1-(4,4-difluorocyclohexyl)piperidin-4-yl]-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{[4-(morpholin-4-yl)piperidin-1-yl]methyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-{[4-(morpholin-4-yl)piperidin-1-yl]methyl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-{4-[(4-cyclopropylpiperazin-1-yl)methyl]phenyl}-*N*-(methanesulfonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[1-(propan-2-yl)piperidin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[1-(oxan-4-yl)piperidin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-{1-[(oxan-4-yl)methyl]piperidin-4-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{1-[(oxan-4-yl)methyl]piperidin-4-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-{1-[(2,5-dimethoxyoxolan-3-yl)methyl]piperidin-4-yl}-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[1-(3,3,3-trifluoropropyl)piperidin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[1-(3,3,3-trifluoropropyl)piperidin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-(4-hydroxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

methyl {3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamate;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[4-(2-methoxyethyl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[3-(morpholin-4-yl)pyrrolidine-1-sulfonyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(4-cyclopropylpiperazine-1-sulfonyl)-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-[4-(2-methoxyethyl)piperazine-1-sulfonyl]-4-[4-(methoxymethyl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-[1-(propan-2-yl)piperidin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[1-(oxan-4-yl)piperidin-4-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[1-(cyclopropylmethyl)piperidin-4-yl]-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[9-(oxetan-3-yl)-3,9-diazaspiro[5.5]undecan-3-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[4-(oxetan-3-yl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[(1-cyclopropylpiperidin-4-yl)methoxy]-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[(1-cyclobutylpiperidin-4-yl)methoxy]-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-[(1-cyclohexylpiperidin-4-yl)methoxy]-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{[1-(oxan-4-yl)piperidin-4-yl]methoxy}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-{1-[(2,5-dimethoxyoxolan-3-yl)methyl]piperidin-4-yl}-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-{2-[(propan-2-yl)oxy]pyrimidin-4-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(2-ethoxypyrimidin-4-yl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(2,2-difluoro-2*H*-1,3-benzodioxol-5-yl)-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(4-methylpiperazine-1-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[1-(propan-2-yl)octahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-(1-cyclobutyloctahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl)-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[1-(oxetan-3-yl)octahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-[1-(oxan-4-yl)octahydro-5*H*-pyrrolo[3,2-*c*]pyridin-5-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-*N*-(methylsulfamoyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-*N*-sulfamoyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-[4-(hexahydropyrrolo[3,4-*c*]pyrrole-2(1*H*)-carbonyl)phenyl]-*N*-(methanesulfonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(azetidine-1-sulfonyl)-3-cyclobutyl-1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-(4-{[3-(dimethylamino)azetidin-1-yl]methyl}phenyl)-*N*-(methanesulfonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-3-[(propan-2-yl)oxy]-4-(4-{[4-(propan-2-yl)piperazin-1-yl]methyl}phenyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-{4-[(4-methoxypiperidin-1-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-{4-[(5-methylhexahydropyrrolo[3,4-*c*]pyrrol-2(1*H*)-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-[4-(5-methylhexahydropyrrolo[3,4-*c*]pyrrole-2(1*H*)-carbonyl)phenyl]-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methylsulfamoyl)-4-{4-[4-(propan-2-yl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

4-[4-(4-cyano-1-methylpiperidin-4-yl)phenyl]-1-cyclohexyl-*N*-(methanesulfonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-{4-[3-(dimethylamino)azetidine-1-carbonyl]phenyl}-*N*-(methanesulfonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-*N*-(methanesulfonyl)-4-{4-[(8-methyl-2-oxa-5,8-diazaspiro[3.5]nonan-5-yl)methyl]phenyl}-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-{4-[(4-ethylpiperazin-1-yl)methyl]phenyl}-*N*-(methanesulfonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-cyclohexyl-4-(4-{[4-(dimethylamino)piperidin-1-yl]methyl}phenyl)-*N*-(methanesulfonyl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

1-(4-fluorophenyl)-*N*-(methanesulfonyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-3-[(propan-2-yl)oxy]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(3-methoxyazetidine-1-sulfonyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(3-fluoroazetidine-1-sulfonyl)-1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-*N*-(morpholine-4-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(morpholin-4-yl)cyclohexyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)cyclohexyl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-4-(4-fluoro[1,4'-bipiperidin]-1'-yl)-1-(4-fluorophenyl)-*N*-(methylsulfamoyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

N-(azetidine-1-sulfonyl)-3-cyclobutyl-1-(4-fluorophenyl)-4-{4-[4-(propan-2-yl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-[3-(difluoromethoxy)phenyl]-*N*-(dimethylsulfamoyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(methanesulfonyl)-*N*-methyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-*N*-methyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(ethanesulfonyl)-*N*-methyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-*N*-(ethanesulfonyl)-*N*-methyl-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

2-(3-cyclobutyl-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl)-6-methyl-1λ^6,2,6-thiadiazinane-1,1-dione;

2-(3-cyclobutyl-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl)-1λ^6,2-thiazolidine-1,1-dione;

3-cyclobutyl-*N*-(methanesulfonyl)-*N*-methyl-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

2-(3-cyclobutyl-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl)-1λ^6,2-thiazinane-1,1-dione;

2-{3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}-6-methyl-1λ^6,2,6-thiadiazinane-1,1-dione;

2-{3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}-1λ^6,2-thiazolidine-1,1-dione;

2-{3-cyclobutyl-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}-1λ^6,2-thiazinane-1,1-dione;

2-{3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}-1λ^6,2-thiazolidine-1,1-dione;

2-{3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}-1λ^6,2-thiazinane-1,1-dione;

3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-(methylsulfamoyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(2-methoxyethanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-(morpholine-4-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-*N*-(3-hydroxypropane-1-sulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

ethyl 4-[({3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)amino]piperidine-1-carboxylate;

3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[(oxetan-3-yl)sulfamoyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[(oxan-4-yl)sulfamoyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-*N*-[4-(morpholin-4-yl)piperidine-1-sulfonyl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide;

ethyl 4-{3-cyclobutyl-1-(4-fluorophenyl)-6-[(2-methoxyethanesulfonyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperazine-1-carboxylate;

ethyl 4-{3-cyclobutyl-1-(4-fluorophenyl)-6-[(morpholine-4-sulfonyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperazine-1-carboxylate;

ethyl 4-{3-cyclobutyl-1-(4-fluorophenyl)-6-[(methanesulfonyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperazine-1-carboxylate;

ethyl 4-{3-cyclobutyl-1-(4-fluorophenyl)-6-[(methylsulfamoyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperazine-1-carboxylate;

2-methylpropyl 4-{3-cyclobutyl-1-(4-fluorophenyl)-6-[(methanesulfonyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperazine-1-carboxylate;

2-methylpropyl 4-{3-cyclobutyl-1-(4-fluorophenyl)-6-[(morpholine-4-sulfonyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperazine-1-carboxylate;

2-methylpropyl 4-{3-cyclobutyl-1-(4-fluorophenyl)-6-[(2-methoxyethanesulfonyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperazine-1-carboxylate;

2-methylpropyl 4-{3-cyclobutyl-1-(4-fluorophenyl)-6-[(methylsulfamoyl)carbamoyl]-1*H*-pyrazolo[3,4-*b*]pyridin-4-yl}piperazine-1-carboxylate;

3-cyclobutyl-1-(4-fluorophenyl)-4-(9-methyl-3,9-diazaspiro[5.5]undecan-3-yl)-*N*-(morpholine-4-sulfonyl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide; and

N-(2-aminopyridine-3-sulfonyl)-3-cyclobutyl-1-(4-fluorophenyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide.

33. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier.

34. A compound of claim 1 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 33, for use in medicine.

35. A compound of claim 1 or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 33, for use in the treatment of cystic fibrosis.

36. Use of a compound of claim 1 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cystic fibrosis in a subject in need thereof.

37. A pharmaceutical composition comprising a compound of claim 1 or a pharmaceutically acceptable salt thereof, one potentiator, and one or more additional correctors.

38. Use of a compound of claim 1 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cystic fibrosis in a subject in need thereof, wherein the medicament is to be administered with one potentiator, and one or more additional correctors.

39. A pharmaceutical composition comprising a compound of claim 1 or a pharmaceutically acceptable salt thereof, and one or more additional therapeutic agents.

40. The pharmaceutical composition of claim 39 wherein the additional therapeutic agents are selected from the group consisting of CFTR modulators and CFTR amplifiers.

41. The pharmaceutical composition of claim 39 wherein the additional therapeutic agents are CFTR modulators.

42. Use of a compound of claim 1 or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating cystic fibrosis in a subject in need thereof, wherein the medicament is to be admininstered with one or more additional therapeutic agents.

43. The use of claim 42 wherein the additional therapeutic agents are selected from the group consisting of CFTR modulators, corrected CFTR stabilizers and CFTR amplifiers.

44. The use of claim 42 wherein the additional therapeutic agents are CFTR modulators.

45. Benzyl 3-({3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine-6-carbonyl}sulfamoyl)pyrrolidine-1-carboxylate, or a pharmaceutically acceptable salt thereof.

46. 3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[2-(methoxymethyl)morpholin-4-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide, or a pharmaceutically acceptable salt thereof.

47. 3-cyclobutyl-*N*-(morpholine-4-sulfonyl)-1-phenyl-4-{4-[(pyrrolidin-1-yl)methyl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide, or a pharmaceutically acceptable salt thereof.

48. 3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-(4-methoxy[1,4'-bipiperidin]-1'-yl)-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide, or a pharmaceutically acceptable salt thereof.

49. 3-cyclobutyl-*N*-(dimethylsulfamoyl)-1-(4-fluorophenyl)-4-{4-[4-(propan-2-yl)piperazin-1-yl]piperidin-1-yl}-1*H*-pyrazolo[3,4-*b*]pyridine-6-carboxamide, or a pharmaceutically acceptable salt thereof.

50. 3-cyclobutyl-N-(morpholine-4-sulfonyl)-4-[4-(morpholin-4-yl)piperidin-1-yl]-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxamide, or a pharmaceutically acceptable salt thereof.

51. 3-cyclobutyl-N-(methanesulfonyl)-4-[4-(methoxymethyl)piperidin-1-yl]-1-(2-methoxypyridin-4-yl)-1H-pyrazolo[3,4-b]pyridine-6-carboxamide, or a pharmaceutically acceptable salt thereof.

52. N-(2-acetamidoethanesulfonyl)-3-cyclobutyl-4-[4-(methoxymethyl)piperidin-1-yl]-1-phenyl-1H-pyrazolo[3,4-b]pyridine-6-carboxamide, or a pharmaceutically acceptable salt thereof.