FACTOR XIIA INHIBITORS

This invention relates to enzyme inhibitors that are inhibitors of Factor XIIa (FXIIa), and to pharmaceutical compositions comprising, and uses of, such inhibitors.

Background to the invention

The compounds of the present invention are inhibitors of factor XIIa (FXIIa) and thus have a number of possible therapeutic applications, particularly in the treatment of diseases or conditions in which factor XIIa inhibition is implicated.

FXIIa is a serine protease (EC 3.4.21.38) derived from its zymogen precursor, factor XII (FXII), which is expressed by the *F12* gene. Single chain FXII has a low level of amidolytic activity that is increased upon interaction with negatively charged surfaces and has been implicated in its activation (see Invanov et al., Blood. 2017 Mar 16;129(11):1527-1537. doi: 10.1182/blood-2016-10-744110). Proteolytic cleavage of FXII to heavy and light chains of FXIIa dramatically increases catalytic activity. FXIIa that retains its full heavy chain is αFXIIa. FXIIa that retains a small fragment of its heavy chain is βFXIIa. The separate catalytic activities of αFXIIa and βFXIIa contribute to the activation and biochemical functions of FXIIa. Mutations and polymorphisms in the *F12* gene can alter the cleavage of FXII and FXIIa.

FXIIa has a unique and specific structure that is different from many other serine proteases. For instance, the Tyr99 in FXIIa points towards the active site, partially blocking the S2 pocket and giving it a closed characteristic. Other serine proteases containing a Tyr99 residue (e.g. FXa, tPA and FIXa) have a more open S2 pocket. Moreover, in several trypsin-like serine proteases the P4 pocket is lined by an "aromatic box" which is responsible for the P4-driven activity and selectivity of the corresponding inhibitors. However, FXIIa has an incomplete "aromatic box" resulting in more open P4 pocket. See e.g. *"Crystal structures of the recombinant β-factor XIIa protease with bound Thr-Arg and Pro-Arg substrate mimetics"* M. Pathak et al., Acta. Cryst.2019, D75, 1-14; *"Structures of human plasma β–factor XIIa cocrystallized with potent inhibitors"* A Dementiev et al., Blood Advances 2018, 2(5), 549-558; *"Design of Small-Molecule Active-Site Inhibitors of the S1A Family Proteases as Procoagulant and Anticoagulant Drugs"* P. M. Fischer, J. Med. Chem., 2018, 61(9), 3799-3822; *"Assessment of the protein interaction between coagulation factor XII and corn trypsin inhibitor by molecular docking and biochemical validation"* B. K. Hamad et al. Journal of Thrombosis and Haemostasis, 15: 1818–1828.

FXIIa converts plasma prekallikrein (PK) to plasma kallikrein (PKa), which provides positive feedback activation of FXII to FXIIa. FXII, PK, and high molecular weight kininogen (HK) together represent the contact system. FXIIa mediated conversion of plasma prekallikrein to plasma kallikrein can cause subsequent cleavage of HK to generate bradykinin, a potent inflammatory hormone that can also increase vascular permeability, which has been implicated in disorders such as hereditary angioedema (HAE). The contact system is activated via a number of mechanisms, including interactions with negatively charged surfaces, negatively charged molecules, unfolded proteins, artificial surfaces, foreign tissue (e.g. biological transplants, that include bio-prosthetic heart valves, and organ/tissue transplants), bacteria, and biological surfaces (including endothelium and extracellular matrix) that mediate assembly of contact system components. In addition, the contact system is activated by plasmin, and cleavage of FXII by other enzymes can facilitate its activation.

Activation of the contact system leads to activation of the kallikrein kinin system (KKS), complement system, and intrinsic coagulation pathway (see https://www.genome.jp/kegg-bin/show_pathway?map04610). In addition, FXIIa has additional substrates both directly, and indirectly via PKa, including Proteinase-activated receptors (PARs), plasminogen, and neuropeptide Y (NPY) which can contribute to the biological activity of FXIIa. Inhibition of FXIIa could provide clinical benefits by treating diseases and conditions associated with these systems, pathways, receptors, and hormones.

PKa activation of PAR2 mediates neuroinflammation and may contribute to neuroinflammatory disorders including multiple sclerosis (see Göbel et al., Proc Natl Acad Sci U S A. 2019 Jan 2;116(1):271-276. doi: 10.1073/pnas.1810020116). PKa activation of PAR1 and PAR2 on vascular smooth muscle cells has been implicated in vascular hypertrophy and atherosclerosis (see Abdallah et al., J Biol Chem. 2010 Nov 5;285(45):35206-15. doi: 10.1074/jbc.M110.171769). FXIIa activation of plasminogen to plasmin contributes to fibrinolysis (see Konings et al., Thromb Res. 2015 Aug;136(2):474-80. doi: 10.1016/j.thromres.2015.06.028). PKa proteolytically cleaves NPY and thereby alters its binding to NPY receptors (Abid et al., J Biol Chem. 2009 Sep 11;284(37):24715-24. doi: 10.1074/jbc.M109.035253). Inhibition of FXIIa could provide clinical benefits by treating diseases and conditions caused by PAR signaling, NPY metabolism, and plasminogen activation.

FXIIa-mediated activation of the KKS results in the production of bradykinin (BK), which can mediate, for example, angioedema, pain, inflammation, vascular hyperpermeability, and vasodilatation (see Kaplan et al., Adv Immunol. 2014;121:41-89. doi: 10.1016/B978-0-12-800100-4.00002-7; and Hopp et al., J Neuroinflammation. 2017 Feb 20;14(1):39. doi: 10.1186/s12974-017-0815-8). Garadacimab (CSL-312), a monoclonal antibody inhibitory against FXIIa, recently completed a phase 2 study where monthly

prophylactic subcutaneous treatment was reported to be well tolerated and effective in preventing attacks in patients with type I/II hereditary angioedema (HAE), which results in intermittent swelling of face, hands, throat, gastro-intestinal tract and genitals (see https://www.clinicaltrials.gov/ct2/show/NCT03712228 and Craig et al., 1451, Allergy. 2020;75(Suppl. 109):5–99. doi: 10.1111/all.14504). Mutations in FXII that facilitate its activation to FXIIa have been identified as a cause of HAE (see Björkqvist et al., J Clin Invest. 2015 Aug 3;125(8):3132-46. doi: 10.1172/JCI77139; and de Maat et al., J Allergy Clin Immunol. 2016 Nov;138(5):1414-1423.e9. doi: 10.1016/j.jaci.2016.02.021). Since FXIIa mediates the generation of PK to PKa, inhibitors of FXIIa could provide protective effects of all form of BK-mediated angioedema, including HAE and non-hereditary bradykinin-mediated angioedema (BK-AEnH).

"Hereditary angioedema" can be defined as any disorder characterised by recurrent episodes of bradykinin-mediated angioedema (e.g. severe swelling) caused by an inherited genetic dysfunction/fault/mutation. There are currently three known categories of HAE: (i) HAE type 1, (ii) HAE type 2, and (iii) normal C1 inhibitor HAE (normal C1-Inh HAE). However, work on characterizing the etiologies of HAE is ongoing so it is expected that further types of HAE might be defined in the future.

Without wishing to be bound by theory, it is thought that HAE type 1 is caused by mutations in the SERPING1 gene that lead to reduced levels of C1 inhibitor in the blood. Without wishing to be bound by theory, it is thought that HAE type 2 is caused by mutations in the SERPING1 gene that lead to dysfunction of the C1 inhibitor in the blood. Without wishing to be bound by theory, the cause of normal C1-Inh HAE is less well defined and the underlying genetic dysfunction/fault/mutation can sometimes remain unknown. What is known is that the cause of normal C1-Inh HAE is not related to reduced levels or dysfunction of the C1 inhibitor (in contrast to HAE types 1 and 2). Normal C1-Inh HAE can be diagnosed by reviewing the family history and noting that angioedema has been inherited from a previous generation (and thus it is hereditary angioedema). Normal C1-Inh HAE can also be diagnosed by determining that there is a dysfunction/fault/mutation in a gene other than those related to C1 inhibitor. For example, it has been reported that dysfunction/fault/mutation with plasminogen can cause normal C1-Inh HAE (see e.g. Veronez et al., Front Med (Lausanne). 2019 Feb 21;6:28. doi: 10.3389/fmed.2019.00028; or Recke et al., Clin Transl Allergy. 2019 Feb 14;9:9. doi: 10.1186/s13601-019-0247-x.). It has also been reported that dysfunction/fault/mutation with Factor XII can cause normal C1-Inh HAE (see e.g. Mansi et al. 2014 The Association for the Publication of the Journal of Internal Medicine Journal of Internal Medicine, 2015, 277; 585–593; or Maat et al. J Thromb Haemost. 2019 Jan;17(1):183-194. doi: 10.1111/jth.14325).

However, angioedemas are not necessarily inherited. Indeed, another class of angioedema is bradykinin mediated angioedema non-hereditary (BK-AEnH), which is not caused by an inherited genetic dysfunction/fault/mutation. Often the underlying cause of BK-AEnH is unknown and/or undefined. However, the signs and symptoms of BK-AEnH are similar to those of HAE, which, without being bound by theory, is thought to be on account of the shared bradykinin mediated pathway between HAE and BK-AEnH. Specifically, BK-AEnH is characterised by recurrent acute attacks where fluids accumulate outside of the blood vessels, blocking the normal flow of blood or lymphatic fluid and causing rapid swelling of tissues such as in the hands, feet, limbs, face, intestinal tract, airway or genitals.

Specific types of BK-AEnH include: non hereditary angioedema with normal C1 Inhibitor (AE-nC1 Inh), which can be environmental, hormonal, or drug induced; acquired angioedema; anaphylaxis associated angioedema; angiotensin converting enzyme (ACE) inhibitor induced angioedema; dipeptidyl peptidase 4 inhibitor induced angioedema; and tPA induced angioedema (tissue plasminogen activator induced angioedema). However, reasons why these factors and conditions cause angioedema in only a relatively small proportion of individuals are unknown.

Environmental factors that can induce AE-nC1 Inh include air pollution (Kedarisetty et al, Otolaryngol Head Neck Surg. 2019 Apr 30:194599819846446. doi: 10.1177/0194599819846446) and silver nanoparticles such as those used as antibacterial components in healthcare, biomedical and consumer products (Long et al., Nanotoxicology. 2016;10(4):501-11. doi: 10.3109/17435390.2015.1088589).

Various publications suggest a link between the bradykinin and contact system pathways and BK-AEnHs, and also the potential efficacy of treatments, see e.g.: Bas et al. (N Engl J Med 2015; Leibfried and Kovary. J Pharm Pract 2017); van den Elzen et al. (Clinic Rev Allerg Immunol 2018); Han et al (JCI 2002).

For instance, BK-medicated AE can be caused by thrombolytic therapy. For example, tPA induced angioedema is discussed in various publications as being a potentially life threatening complication following thrombolytic therapy in acute stroke victims (see e.g. Simão et al., Blood. 2017 Apr 20;129(16):2280-2290. doi: 10.1182/blood-2016-09-740670; Fröhlich et al., Stroke. 2019 Jun 11:STROKEAHA119025260. doi: 10.1161/STROKEAHA.119.025260; Rathbun, Oxf Med Case Reports. 2019 Jan 24;2019(1):omy112. doi: 10.1093/omcr/omy112; Lekoubou et al., Neurol Res. 2014 Jul;36(7):687-94. doi: 10.1179/1743132813Y.0000000302; Hill et al., Neurology. 2003 May 13;60(9):1525-7).

Stone et al. (Immunol Allergy Clin North Am. 2017 Aug;37(3):483-495.) reports that certain drugs can cause angioedema.

Scott et al. (Curr Diabetes Rev. 2018;14(4):327-333. doi: 10.2174/1573399813666170214113856) reports cases of dipeptidyl Peptidase-4 Inhibitor induced angioedema.

Hermanrud et al., (BMJ Case Rep. 2017 Jan 10;2017. pii: bcr2016217802) reports recurrent angioedema associated with pharmacological inhibition of dipeptidyl peptidase IV and also discusses acquired angioedema related to angiotensin-converting enzyme inhibitors (ACEI-AAE). Kim et al. (Basic Clin Pharmacol Toxicol. 2019 Jan;124(1):115-122. doi: 10.1111/bcpt.13097) reports angiotensin II receptor blocker (ARB)-related angioedema. Reichman et al., (Pharmacoepidemiol Drug Saf. 2017 Oct;26(10):1190-1196. doi: 10.1002/pds.4260) also reports angioedema risk for patients taking ACE inhibitors, ARB inhibitors and beta blockers. Diestro et al. (J Stroke Cerebrovasc Dis. 2019 May;28(5):e44-e45. doi: 10.1016/j.jstrokecerebrovasdis.2019.01.030) also reports a possible association between certain angioedemas and ARBs.

Giard et al. (Dermatology. 2012;225(1):62-9. doi: 10.1159/000340029) reports that bradykinin mediated angioedema can be precipitated by estrogen contraception, so called “oestrogen associated angioedema”.

Contact system mediated activation of the KKS has also been implicated in retinal edema and diabetic retinopathy (see Liu et al., Biol Chem. 2013 Mar;394(3):319-28. doi: 10.1515/hsz-2012-0316). FXIIa concentrations are increased in the vitreous fluid from patients with advance diabetic retinopathy and in Diabetic Macular Edema (DME) (see Gao et al., Nat Med. 2007 Feb;13(2):181-8. Epub 2007 Jan 28 and Gao et al., J Proteome Res. 2008 Jun;7(6):2516-25. doi: 10.1021/pr800112g). FXIIa has been implicated in mediating both vascular endothelial growth factor (VEGF) independent DME (see Kita et al., Diabetes. 2015 Oct;64(10):3588-99. doi: 10.2337/db15-0317) and VEGF mediated DME (see Clermont et al., Invest Ophthalmol Vis Sci. 2016 May 1;57(6):2390-9. doi: 10.1167/iovs.15-18272). FXII deficiency is protective against VEGF induced retinal edema in mice (Clermont et al., ARVO talk 2019). Therefore, it has been proposed that FXIIa inhibition will provide therapeutic effects for diabetic retinopathy and retinal edema caused by retinal vascular hyperpermeability, including DME, retinal vein occlusion, age-related macular degeneration (AMD).

As noted above, the contact system can be activated by interaction with bacteria, and therefore FXIIa has been implicated in the treatment of sepsis and bacterial sepsis (see Morrison et al., J Exp Med. 1974 Sep 1;140(3):797-811). Therefore, FXIIa inhibitors could provide therapeutic benefits in treating sepsis, bacterial sepsis and disseminated intravascular coagulation (DIC).

FXIIa mediated activation of the KKS and production of BK have been implicated in neurodegenerative diseases including Alzheimer's disease, multiple sclerosis, epilepsy and migraine (see Zamolodchikov et al., Proc Natl Acad Sci U S A. 2015 Mar 31;112(13):4068-73. doi: 10.1073/pnas.1423764112; Simões et al., J Neurochem. 2019 Aug;150(3):296-311. doi: 10.1111/jnc.14793; Göbel et al., Nat Commun. 2016 May 18;7:11626. doi: 10.1038/ncomms11626; and https://clinicaltrials.gov/ct2/show/NCT03108469). Therefore, FXIIa inhibitors could provide therapeutic benefits in reducing the progression and clinical symptoms of these neurodegenerative diseases.

FXIIa has also been implicated in anaphylaxis (see Bender et al., Front Immunol. 2017 Sep 15;8:1115. doi: 10.3389/fimmu.2017.01115; and Sala-Cunill et al., J Allergy Clin Immunol. 2015 Apr;135(4):1031-43.e6. doi: 10.1016/j.jaci.2014.07.057). Therefore, FXIIa inhibitors could provide therapeutic benefits in reducing the clinical severity and incidence of anaphylactic reactions.

The role of FXIIa in coagulation was identified over 50 years ago, and has been extensively documented in publications using biochemical, pharmacological, genetic and molecular studies (see Davie et al., Science. 1964 Sep 18;145(3638):1310-2). FXIIa mediated activation of factor XI (FXI) triggers the intrinsic coagulation pathway. In addition, FXIIa can increase coagulation in a FXI independent manner (see Radcliffe et al., Blood. 1977 Oct;50(4):611-7; and Puy et al., J Thromb Haemost. 2013 Jul;11(7):1341-52. doi: 10.1111/jth.12295). Studies on both humans and experimental animal models have demonstrated that FXII deficiency prolongs activated partial prothrombin time (APTT) without adversely affecting hemostasis (see Renné et al., J Exp Med. 2005 Jul 18;202(2):271-81; and Simão et al., Front Med (Lausanne). 2017 Jul 31;4:121. doi: 10.3389/fmed.2017.00121). Pharmacological inhibition of FXIIa also prolongs APTT without increasing bleeding (see Worm et al., Ann Transl Med. 2015 Oct;3(17):247. doi: 10.3978/j.issn.2305-5839.2015.09.07). These data suggest that inhibition of FXIIa could provide therapeutic effects against thrombosis without inhibiting bleeding. Therefore, FXIIa inhibitors could be used to treat a spectrum of prothrombotic conditions including venous thromboembolism (VTE); cancer associated thrombosis; complications caused by mechanical and bioprosthetic heart valves, catheters, extracorporeal membrane oxygenation (ECMO), left ventricular assisted devices (LVAD), dialysis, cardiopulmonary bypass (CPB); sickle cell disease, joint arthroplasty, thrombosis induced by tPA, Paget-Schroetter syndrome and Budd-Chari syndrome. FXIIa inhibitor could be used for the treatment and/or prevention of thrombosis, edema, and inflammation associated with these conditions.

Surfaces of medical devices that come into contact with blood can cause thrombosis. FXIIa inhibitors may also be useful for treating or preventing thromboembolism by lowering the propensity of devices that

come into contact with blood to clot blood. Examples of devices that come into contact with blood include vascular grafts, stents, in-dwelling catheters, external catheters, orthopedic prosthesis, cardiac prosthesis, and extracorporeal circulation systems.

Preclinical studies have shown that FXIIa has been shown to contribute to stroke and its complications following both ischemic stroke, and hemorrhagic accidents (see Barbieri et al., J Pharmacol Exp Ther. 2017 Mar;360(3):466-475. doi: 10.1124/jpet.116.238493; Krupka et al., PLoS One. 2016 Jan 27;11(1):e0146783. doi: 10.1371/journal.pone.0146783; Leung et al., Transl Stroke Res. 2012 Sep;3(3):381-9. doi: 10.1007/s12975-012-0186-5; Simão et al., Blood. 2017 Apr 20;129(16):2280-2290. doi: 10.1182/blood-2016-09-740670; and Liu et al., Nat Med. 2011 Feb;17(2):206-10. doi: 10.1038/nm.2295). Therefore, FXIIa inhibition may improve clinical neurological outcomes in the treatment of patients with stroke.

FXII deficiency has been shown to reduce the formation of atherosclerotic lesions in *Apoe*$^{-/-}$ mice (Didiasova et al., Cell Signal. 2018 Nov;51:257-265. doi: 10.1016/j.cellsig.2018.08.006). Therefore, FXIIa inhibitors could be used in the treatment of atherosclerosis.

FXIIa, either directly, or indirectly via PKa, has been shown to activate the complement system (Ghebrehiwet et al., Immunol Rev. 2016 Nov;274(1):281-289. doi: 10.1111/imr.12469). BK increases complement C3 in the retina, and an in vitreous increase in complement C3 is associated with DME (Murugesan et al., Exp Eye Res. 2019 Jul 24;186:107744. doi: 10.1016/j.exer.2019.107744). Both FXIIa and PKa activate the complement system (see Irmscher et al., J Innate Immun. 2018;10(2):94-105. doi: 10.1159/000484257; and Ghebrehiwet et al., J Exp Med. 1981 Mar 1;153(3):665-76).

A phase 2 study to assess the safety and efficacy of CSL312, a FXIIa inhibitor, in the treatment of COVID-19 has been assigned clinicaltrials.gov identifier NCT04409509. Shatzel et al. (Res Pract Thromb Haemost, 2020 May 15;4(4):500-505. doi: 10.1002/rth2.12349) also relates to investigating the contact system's role in COVID-19.

Wygrecka et al. ("Coagulation factor XII regulates inflammatory responses in human lungs", European Respiratory Journal 2017 50: PA339; DOI: 10.1183/1393003.congress-2017.PA339) relates to the effect of an accumulation of FXII in acute respiratory distress syndrome (ARDS) lungs.

Wong et al. ("CSL312, a Novel Anti-FXII Antibody, Blocks FXII-Induced IL-6 Production from Primary Non-Diseased and Idiopathic Pulmonary Fibrosis Fibroblasts", American Journal of Respiratory and Critical Care

Medicine 2020;201:A6363) reports that activated FXII may contribute to lung fibrosis (e.g. idiopathic Pulmonary Fibrosis) through direct stimulation of fibroblasts to produce pro-fibrotic cytokine IL-6.

Göbel et al. (The Coagulation Factors Fibrinogen, Thrombin, and Factor XII in Inflammatory Disorders—A Systematic Review, Front. Immunol., 26 July 2018| https://doi.org/10.3389/fimmu.2018.01731) relates to FXII's role in the rheumatoid arthritis (RA).

Scheffel et al. (Cold-induced urticarial autoinflammatory syndrome related to factor XII activation, Nature Communications volume 11, Article number: 179 (2020)) reports that there is a link between contact system activation and cytokine-mediated inflammation, such as cold-induced urticarial autoinflammatory syndrome.

Peyrou et al. (The kallikrein–kinin pathway as a mechanism for auto-control of brown adipose tissue activity, NATURE COMMUNICATIONS, (2020) 11:2132, https://doi.org/10.1038/s41467-020-16009-x), reports a pathway for controlling brown adipose tissue (BAT) thermogenic activity mediated by the kallikrein–kinin system, which may contribute to expanding the range of potential pharmacological candidates in therapeutic strategies against obesity and associated diseases designed to improve energy expenditure and remove excess blood metabolites through activation of BAT. Impaired BAT activity is associated with obesity and insulin resistance.

Compounds that are said to be FXIIa inhibitors have been described by Rao et al. ("Factor XIIa Inhibitors" WO2018/093695), Hicks et al. ("Factor XIIa Inhibitors" WO2018/093716), Breslow et al. ("Aminotriazole immunomodulators for treating autoimmune diseases" WO2017/123518) and Ponda et al. ("Aminacylindazole immunomodulators for treatment of autoimmune diseases" WO2017/205296 and "Pyranopyrazole and pyrazolopyridine immunomodulators for treatment of autoimmune diseases" WO2019/108565). FXII/FXIIa inhibitors are said to have been described by Nolte et al. ("Factor XII inhibitors for the administration with medical procedures comprising contact with artificial surfaces" WO2012/120128).

Compounds that are said to be modulators of FXIIa have been described by Philippou et al. ("Factor XIIa Inhibitors" WO 2019/211585 and WO 2019/186164). Macrocylic peptides that are said to be inhibitors of FXIIa have been described by Wilbs et al. (Nat Commun 11, 3890 (2020). Doi: 10.1038/s41467-020-17648-w).

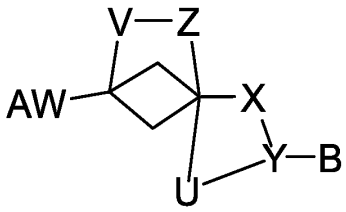
To date, no FXIIa inhibitors have been approved for medical use, and there are no small molecule FXIIa inhibitors in clinical development. Although certain known compounds are said to be modulators or inhibitors of FXIIa, these compounds can suffer from limitations such as being non-reversible or covalent binders, being poorly selective for FXIIa over other related enzymes, or not having demonstrated pharmacokinetic properties suitable for oral therapy. For example, compounds with acylating reactivity e.g. acylated aminotriazoles, are typically non-reversible covalent binders, and can sometimes also be unstable in water and/or blood plasma due to their inherent reactivity. Poor selectivity for FXIIa over other serine proteases (such as thrombin, FXa, FXIa, KLK1, plasmin, trypsin) increases the risk of off-target effects, which can be made even worse (i.e. there is typically a higher likelihood of poor selectivity and off-target effects) if the inhibitor is a covalent binder. Therefore, there remains a need to develop new FXIIa inhibitors that are not covalent inhibitors and/or are highly selective for FXIIa in order to e.g. mitigate the risks of non-selectivity and cytotoxicity. There is a particular need to develop a small molecule FXIIa inhibitors as an oral therapy.

In view of the above, there also remains a need to develop new FXIIa inhibitors that will have utility to treat a wide range of disorders, in particular angioedema; HAE, including : (i) HAE type 1, (ii) HAE type 2, and (iii) normal C1 inhibitor HAE (normal C1-Inh HAE); BK-AEnH, including AE-nC1 Inh, ACE and tPA induced angioedema; vascular hyperpermeability; stroke including ischemic stroke and haemorrhagic accidents; retinal edema; diabetic retinopathy; impaired visual acuity; DME; retinal vein occlusion; AMD; neuroinflammation; neuroinflammatory/neurodegenerative disorders such as MS (multiple sclerosis); other neurodegenerative diseases such as Alzheimer's disease, epilepsy and migraine; sepsis; bacterial sepsis; inflammation; anaphylaxis; thrombosis; thromboembolism caused by increased propensity of medical devices that come into contact with blood to clot blood; prothrombotic conditions including disseminated intravascular coagulation (DIC), venous thromboembolism (VTE), cancer associated thrombosis, complications caused by mechanical and bioprosthetic heart valves, complications caused by catheters, complications caused by ECMO, complications caused by LVAD, complications caused by dialysis, complications caused by CPB, sickle cell disease, joint arthroplasty, thrombosis induced to tPA, Paget-Schroetter syndrome and Budd-Chari syndrome; atherosclerosis; COVID-19; acute respiratory distress syndrome (ARDS); idiopathic pulmonary fibrosis (IPF); rheumatoid arthritis (RA); cold-induced urticarial autoinflammatory syndrome; obesity; and diabetes. In particular, there remains a need to develop new FXIIa inhibitors.

Description of the Invention

The present invention relates to a series of inhibitors of Factor XIIa (FXIIa). The compounds of the invention are potentially useful in the treatment of diseases or conditions in which factor XIIa inhibition is implicated. The invention further relates to pharmaceutical compositions of the inhibitors, to the use of the compositions as therapeutic agents, and to methods of treatment using these compositions.

Specifically, the invention provides compounds of formula (I)



Formula (I),

wherein:

U is absent -C(R16)(R17)-, CH_2C(R16)(R17) or C(R16)(R17)CH_2;

-V-Z- is:

absent, -CH_2-, or -CH_2-O-CH_2; or

V is selected from CH_2, O and NR18, and Z is selected from -C(R16)(R17)-CH_2- and -C(R16)(R17)-; or,

V is selected from -CH_2-C(R16)(R17)- and -C(R16)(R17)-, and Z is selected from CH_2, O and NR18;

wherein R18 is selected from H, alkyl, $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), C(=O)SR19 and SO_2R19;

wherein R19 is selected from alkyl, cycloalkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is selected from a bond, O, CR1R2, C=O and NR12;

Y is, where possible, selected from O, CR1R2, CR1, C=O, N and NR12;

R1 is selected from H, alkyl, alkoxy, OH, halo and NR13R14;

R2 is selected from H and small alkyl;

wherein when one of X or Y is C=O, the other is, where possible, O, CR1R2, CR1, N or NR12;

wherein when X is NR12, Y is, where possible, CR1R2, CR1 or C=O;

wherein when Y is, where possible, NR12 or N, X is a bond, CR1R2 or C=O;

wherein when X is O, Y is, where possible, CR1R2, CR1 or C=O;

wherein when Y, where possible, is O, X is a bond, CR1R2 or C=O;
wherein when X is a bond, Y is, where possible, O, N or NR12;

wherein when U is not absent -V-Z- is absent;

wherein when -V-Z- is not absent, U is absent;

B is selected from:

(i) heteroaryl[a];

(ii) aryl;

(iii) a 5- to 6- membered non-aromatic heterocyclic ring containing one N ring member, which is unsaturated with 1 or 2 double bonds, wherein the non-aromatic heterocyclic ring is optionally substituted by 1, 2 or 3 substituents independently selected from alkyl, alkoxy, aryl[b], OH, OCF_3, halo, oxo, CN, and CF_3; and

(iv) a fused 5,5-, 6,5- or 6,6- bicyclic ring containing an aromatic ring fused to a non-aromatic ring, wherein the bicyclic ring optionally contains one or two N ring members, wherein the fused 5,5-, 6,5- or 6,6- bicyclic ring may be optionally substituted with 1, 2, or 3 substituted by up to three substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, oxo, CN, and CF_3, wherein the 6,5- bicyclic ring may be attached via the 6- or 5- membered ring;

AW- is selected from:
$-(CH_2)_{0-6}$-(CHR15)-$(CH_2)_{0-6}$-A, -(CHR12)-A, -O-(CHR12)-A, $-(CH_2)_{0-6}$-A, $-(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A, $-(CH_2)_{0-6}$-NH-$(CH_2)_{0-6}$-A, $-(CH_2)_{0-6}$-NR12-$(CH_2)_{1-6}$-C(=O)-A, $-(CH_2)_{0-6}$-NH-C(=O)-$(CH_2)_{0-6}$-A, -C(=O)NR12-$(CH_2)_{0-6}$-A, $-(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A, $-(CH_2)_{0-6}$-(phenyl)-$(CH_2)_{0-6}$-A, -NH-SO_2-A and -SO_2-NH-A;

A is a 4- to 15- membered mono-, bi-, or tri- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN;
wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro;
wherein when A is a tricyclic ring system, each of the three rings in the tricyclic ring system is either fused, bridged or spiro to at least one of the other rings in the tricyclic ring system;

wherein when -V-Z- is -CH_2-, U is absent, and AW- is A-(C=O)-, A may not be substituted by -$(CH_2)_0$-heteroaryl;

alkyl is a linear saturated hydrocarbon having up to 10 carbon atoms (C_1-C_{10}) or a branched saturated hydrocarbon of between 3 and 10 carbon atoms (C_3-C_{10}); alkyl may optionally be substituted with 1, 2 or 3 substituents independently selected from (C_1-C_6)alkoxy, OH, -NR13R14, -C(=O)OR13, -C(=O)NR13R14, CN, CF_3, halo;

$alkyl^b$ is a linear saturated hydrocarbon having up to 10 carbon atoms (C_1-C_{10}) or a branched saturated hydrocarbon of between 3 and 10 carbon atoms (C_3-C_{10}); $alkyl^b$ may optionally be substituted with 1, 2 or 3 substituents independently selected from (C_1-C_6)alkoxy, OH, CN, CF_3, halo;

small alkyl is a linear saturated hydrocarbon having up to 4 carbon atoms (C_1-C_4) or a branched saturated hydrocarbon of between 3 and 4 carbon atoms (C_3-C_4); small alkyl may optionally be substituted with 1 or 2 substituents independently selected from (C1-C6)alkoxy, OH, NR13R14, C(=O)OR13, C(=O)NR13R14, CN, CF_3, halo;

aryl is phenyl, biphenyl or naphthyl; aryl may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, methylenedioxy, ethylenedioxy, OH, halo, CN, -$(CH_2)_{0-3}$-O-$heteroaryl^a$, $aryl^b$, -O-$aryl^b$, -$(CH_2)_{1-3}$-$aryl^b$, -$(CH_2)_{0-3}$-$heteroaryl^a$, -C(=O)OR13, -C(=O)NR13R14, -$(CH_2)_{0-3}$-NR13R14, OCF_3 and CF_3;

$aryl^b$ is phenyl, biphenyl or naphthyl; $aryl^b$ may be optionally substituted with 1, 2 or 3 substituents independently selected from $alkyl^b$, alkoxy, OH, halo, CN, and CF_3;

cycloalkyl is a monocyclic saturated hydrocarbon ring of between 3 and 6 carbon atoms (C_3-C_6); cycloalkyl may optionally be substituted with 1 or 2 substituents independently selected from alkyl, (C_1-C_6)alkoxy, OH, CN, CF_3, halo;

alkoxy is a linear O-linked hydrocarbon of between 1 and 6 carbon atoms (C_1-C_6) or a branched O-linked hydrocarbon of between 3 and 6 carbon atoms (C_3-C_6); alkoxy may optionally be substituted with 1 or 2 substituents independently selected from OH, CN, CF_3, and fluoro;

halo is F, Cl, Br, or I;

heteroaryl is a 5- or 6- membered carbon-containing aromatic ring containing one, two or three ring members that are selected from N, NR8, S, and O; heteroaryl may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, CN, and CF_3;

heteroaryl[a] is a 5, 6, 9 or 10 membered mono- or bi-cyclic aromatic ring, containing, where possible, 1, 2, 3 or 4 ring members independently selected from N, NR12, S and O; heteroaryl[a] may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, CN, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b], -C(=O)OR12, -C(=O)NR13R14 and CF_3;

heteroaryl[b] is a 5, 6, 9 or 10 membered mono- or bi-cyclic aromatic ring, containing, where possible, 1, 2 or 3 ring members independently selected from N, NR12, S and O; wherein heteroaryl[b] may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl[b], alkoxy, OH, halo, CN, aryl[b], $-(CH_2)_{1-3}$-aryl[b], and CF_3;

R8 is independently selected from H, alkyl, cycloalkyl, and heterocycloalkyl;

heterocycloalkyl is a non-aromatic carbon-containing monocyclic ring containing 3, 4, 5, or 6, ring members, wherein at least one ring member is independently selected from N, NR12, S, and O; heterocycloalkyl may be optionally be substituted with 1 or 2 substituents independently selected from alkyl, $(C_1$-$C_6)$alkoxy, OH, CN, CF_3, halo;

R12 is independently selected from H, alkyl, and cycloalkyl;

R13 and R14 are independently selected from H, alkyl[b], aryl[b] and heteroaryl[b] or R13 and R14 together with the nitrogen atom to which they are attached form a carbon-containing 4-, 5-, 6- or 7-membered heterocyclic ring, optionally containing an additional heteroatom selected from N, NR12, S, SO, SO_2, and O, which may be saturated or unsaturated with 1 or 2 double bonds and which may be optionally mono- or di-substituted with substituents selected from oxo, alkyl[b], alkoxy, OH, halo and CF_3;

R15 is selected from alkyl, halo, CF_3, CN, OH, alkoxy, NR13R14, and CONR13R14;

R16 and R17 are independently selected from H and small alkyl;

and tautomers, isomers, stereoisomers (including enantiomers, diastereoisomers and racemic and scalemic mixtures thereof), deuterated isotopes, and pharmaceutically acceptable salts and/or solvates thereof;

wherein the compound is not *N*-(2-chlorophenyl)-3-((5-cyano-1*H*-indazol-1-yl)-methyl)-*N*-methylbicyclo-[1.1.1]pentane-1-carboxamide.

The compounds of the formula (I) have been developed to be inhibitors of FXIIa, which as noted above, has a unique and specific binding site and there is a need for small molecule FXIIa inhibitors. Compounds of formula (I) can possess characteristics that can be considered suitable for oral delivery e.g. a suitable oral availability profile. The compounds of formula (I) can also avoid including groups associated with covalent binding properties e.g. groups with acylating reactivity such as acylated aminotriazoles, and thus can provide compounds that are reversible inhibitors, to further reduce the risk of off-target effects and cytotoxicity.

The present invention also provides a prodrug of a compound as herein defined, or a pharmaceutically acceptable salt and/or solvate thereof.

The present invention also provides an N-oxide of a compound as herein defined, or a prodrug or pharmaceutically acceptable salt and/or solvate thereof.

It will be understood that “pharmaceutically acceptable salts and/or solvates thereof” means “pharmaceutically acceptable salts thereof”, “pharmaceutically acceptable solvates thereof”, and “pharmaceutically acceptable solvates of salts thereof”.

The compounds of the present invention can be provided as mixtures of more than one stereoisomer. When provided as a mixture of stereoisomers, one stereoisomer can be present at a purity >90 % relative to the remaining stereoisomers. More specifically, when provided as a mixture of stereoisomers, one stereoisomer can be present at a purity >95 % relative to the remaining stereoisomers.

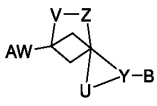
It will be understood that substituents may be named as its free unbonded structure (e.g. piperidine) or by its bonded structure (e.g. piperidinyl). No difference is intended.

It will be understood that the compounds of the invention comprise several substituents. When any of these substituents is defined more specifically herein, the substituents/optional substituents to these groups described above also apply, unless stated otherwise. For example, B can be heteroaryl[a], which more specifically can be isoquinolinyl. In this case, isoquinolinyl can be optionally substituted in the same manner as "heteroaryl[a]".

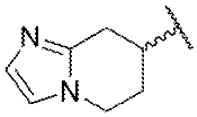
It will be understood that the term "where possible" means that the group, atom, or substituent in question may be present if it is chemically possible to do so, e.g. does not exceed the valencies of chemically stable compounds. For example, Y can, where possible, be N, but only in the instance where U is not absent. This is because, when U is not absent, the N is already trivalent by virtue of its connection to all of X, U and B, and therefore there is no spare valency for a further substituent (such as an R12 group). Likewise, Y can, where possible, be NR12, but only in the instance where U is absent. This is because, when U is absent, the N of the NR12 is connected to X and B, and therefore has one available valency for the R12 group substituent.

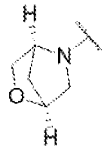
It will be understood that when when U is not absent, -V-Z- is absent, and therefore that pentavalent carbon atoms are not covered by the invention. Similarly, it will be understood that when -V-Z- is not absent, U is absent, and therefore that pentavalent carbon atoms are not covered by the invention. It will be understood that when U is absent, the covalent bonds between U and Y, and between U and the carbon which is attached to X and Z, are also absent. It will be understood from claim 1 that for the carbon which is attached to all of U, X and Z, no configuration of the claim allows for a pentavalent carbon. For example, if -V-Z- is $-CH_2-CH_2-$, U cannot be CH_2 as this would result in the carbon which is attached to all of U, X and Z having five covalent bonds which is not allowable in any configuration of the claim. Therefore, either U, or -V-Z-, and the covalent bonds which attach them must be absent (or both U, -V-Z-, and the covalent bonds which attach them can be absent).

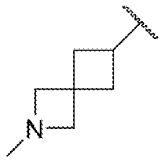
It will be understood that "X is a bond" means that X does not contain an atom, and provides a covalent bond directly from Y to the carbon which is attached to all of U, X and Z. For example, when X is a bond (i.e. Y is connected to the adjacent carbon by X as a covalent bond), the compound of formula (I) is



(with A, W, V, Z, U, Y and B as defined in claim 1).

It will be understood that a fused ring system refers to a ring system where two rings in the ring system share two adjacent atoms (i.e one common covalent bond). For example,  is a fused ring system (specifically a fused bicyclic ring system) which can be considered as an imidazole ring and a piperidine ring sharing a common bond.

It will be understood that a bridged ring system refers to a ring system having two rings sharing three or more atoms. For example,  is a bridged ring system (specifically a bridged bicyclic ring system) which can be considered as a tetrahydrofuran ring and a pyrrolidine ring joined at a bridge and sharing three common atoms.

It will be understood that a spiro ring system refers to a ring system where two rings in the ring system share one common atom. For example,  is a spiro ring system (specifically a spiro bicyclic ring system) which can be considered as a cyclobutane ring and an azetidine ring sharing a common carbon atom.

It will be understood that the ring system A, as defined in formula (I), can be fully saturated, or have any degree of unsaturation. For example, the ring system can be fully saturated, partially unsaturated, aromatic, non-aromatic, or have an aromatic ring bridged, fused or spiro to a non-aromatic ring.

It will be understood that ring system A can contain non-carbon ring members, and that these non-carbon ring members can, where possible, be optionally substituted themselves (as well, or as opposed to the carbon ring members), with the optional substituents included in the definition of A.

It will be understood that when any variable (e.g. alkyl) occurs more than once, its definition on each occurrence is independent of every other occurrence.

It will be understood that combinations of substituents and variables are permissible only if such combinations result in stable compounds.

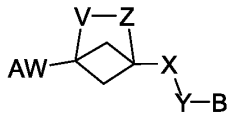
As used herein the term "bradykinin-mediated angioedema" means hereditary angioedema, and any non-hereditary bradykinin-mediated angioedema. For example, "bradykinin-mediated angioedema" encompasses hereditary angioedema and acute bradykinin-mediated angioedema of unknown origin.

As used herein, the term "hereditary angioedema" means any bradykinin-mediated angioedema caused by an inherited genetic dysfunction, fault, or mutation. As a result, the term "HAE" includes at least HAE type 1, HAE type 2, and normal C1 inhibitor HAE (normal C1-Inh HAE).

More specifically, the invention provides compounds of formula (I), or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

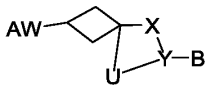
wherein R18 is selected from alkyl, $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), C(=O)SR19 and SO_2R19.

More specifically, the invention also provides compounds of formula (I) wherein U is absent, which are compounds of formula (1a)



Formula (1a).

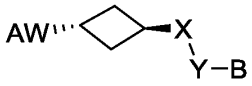
The invention also provides compounds of formula (I) wherein -V-Z- is absent, which are compounds of formula (1b)



Formula (1b).

Specifically, the invention provides compounds of formula (I) wherein when -V-Z- is absent and U is absent, and AW- and -XYB are trans to one another

which are compounds of formula (1c)



Formula (1c)

Preferably, when not absent, -V-Z- is selected from:

$-CH_2-$, or

V is selected from CH_2, O and NR18, and Z is selected from $-C(R16)(R17)-CH_2-$ and $-C(R16)(R17)-$; or,

V is selected from $-CH_2-C(R16)(R17)-$ and $-C(R16)(R17)-$, and Z is selected from CH_2, O and NR18; or

wherein when -V-Z- is absent:

U is absent, CH_2 or $-CH_2CH_2-$.

Preferably, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$; or

when -V-Z- is absent:

U is absent, CH_2 or $-CH_2CH_2-$.

Preferably, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$; or

when -V-Z- is absent:

U is absent, CH_2 or $-CH_2CH_2-$.

Preferably, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$,

$-C(CH_3)_2-O-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$,

$-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$; wherein R18 is selected from:

alkyl, $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), C(=O)SR19 and SO_2R19; or

when -V-Z- is absent:

U is absent, CH_2 or $-CH_2CH_2-$.

Preferably, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$; wherein R18 is selected from:

alkyl, $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), C(=O)SR19 and SO_2R19; or

when -V-Z- is absent:

U is absent, CH_2 or $-CH_2CH_2-$.

Preferably, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or

when -V-Z- is absent:

U is absent, CH_2 or $-CH_2CH_2-$.

Preferably, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

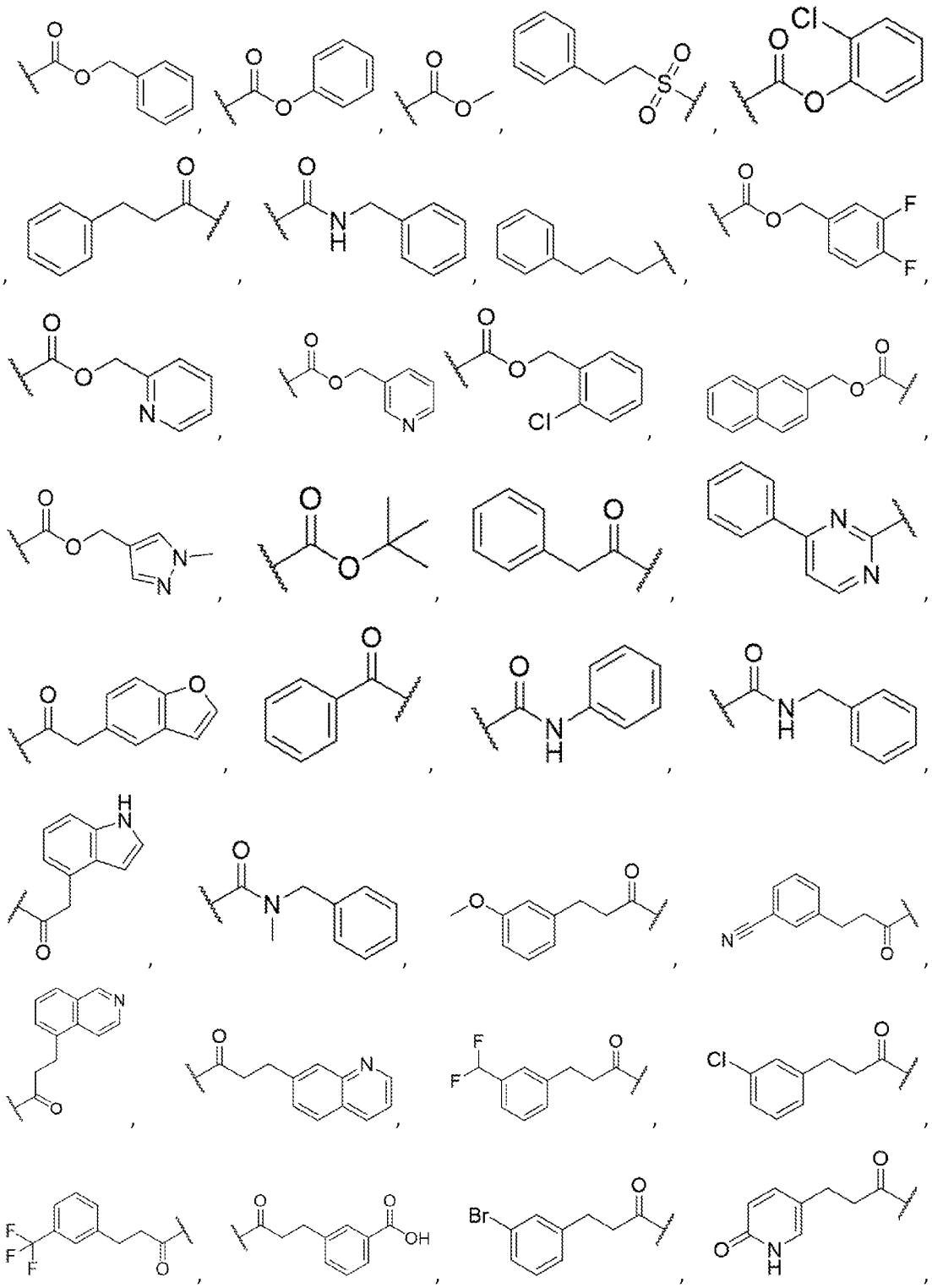
wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or

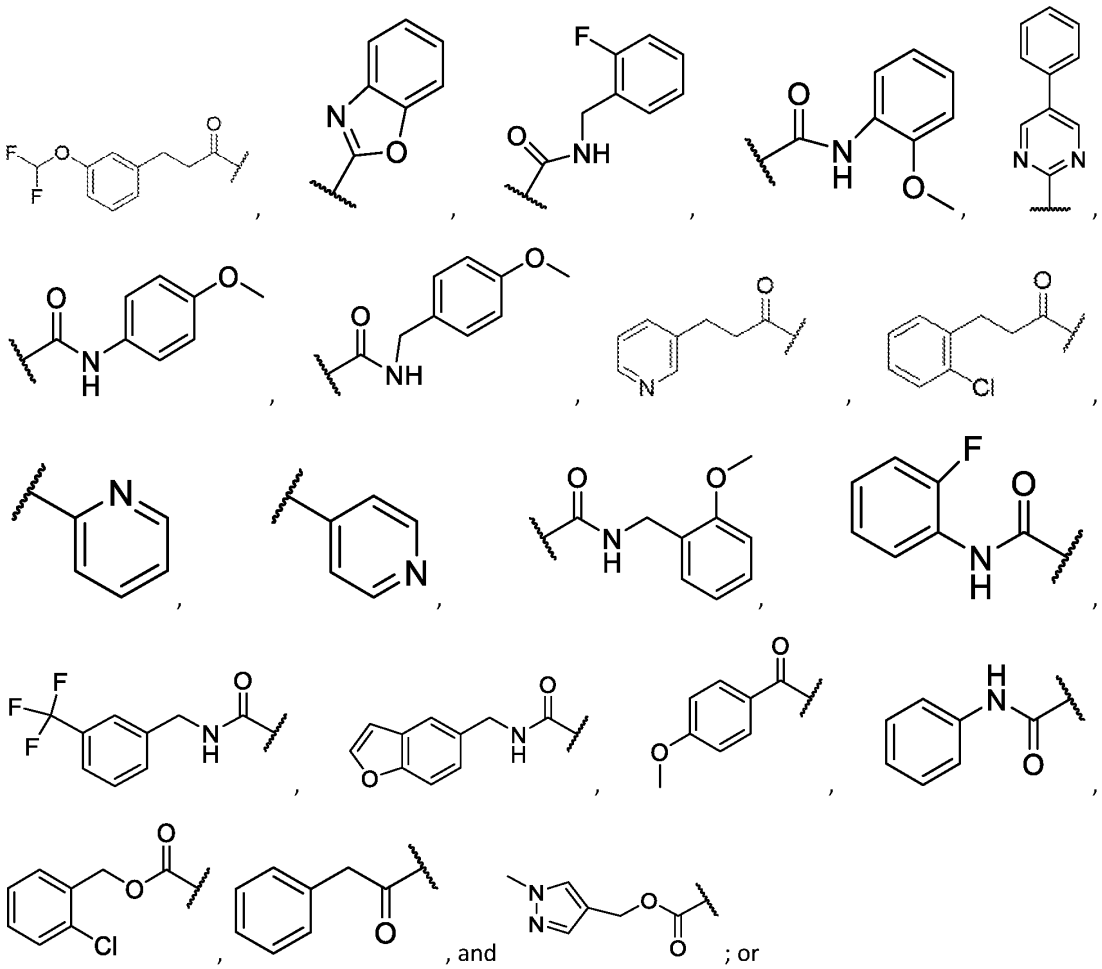
when -V-Z- is absent:

U is absent, CH_2 or $-CH_2CH_2-$.

Preferably, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$ $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$, wherein R18 is selected from:



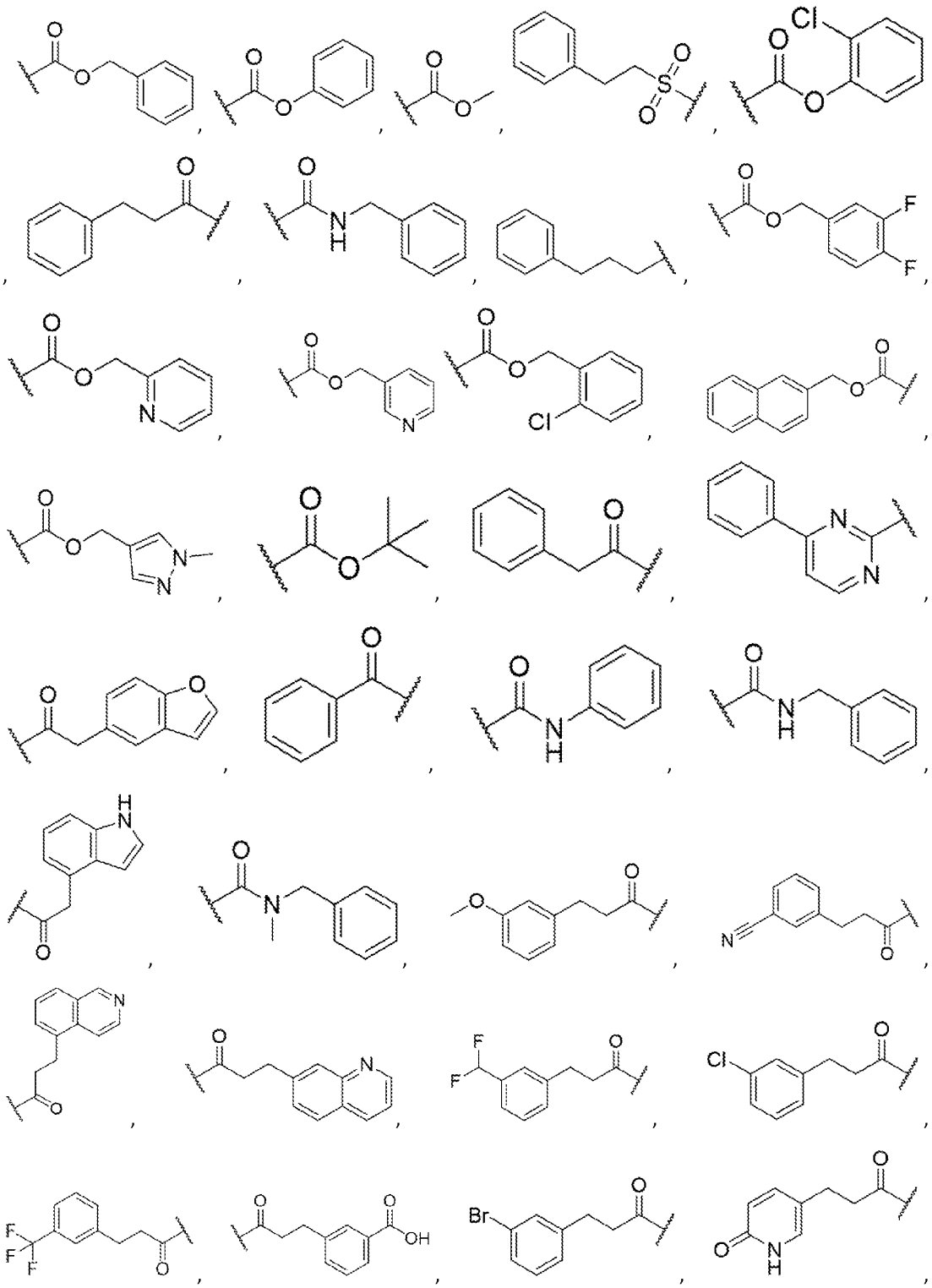


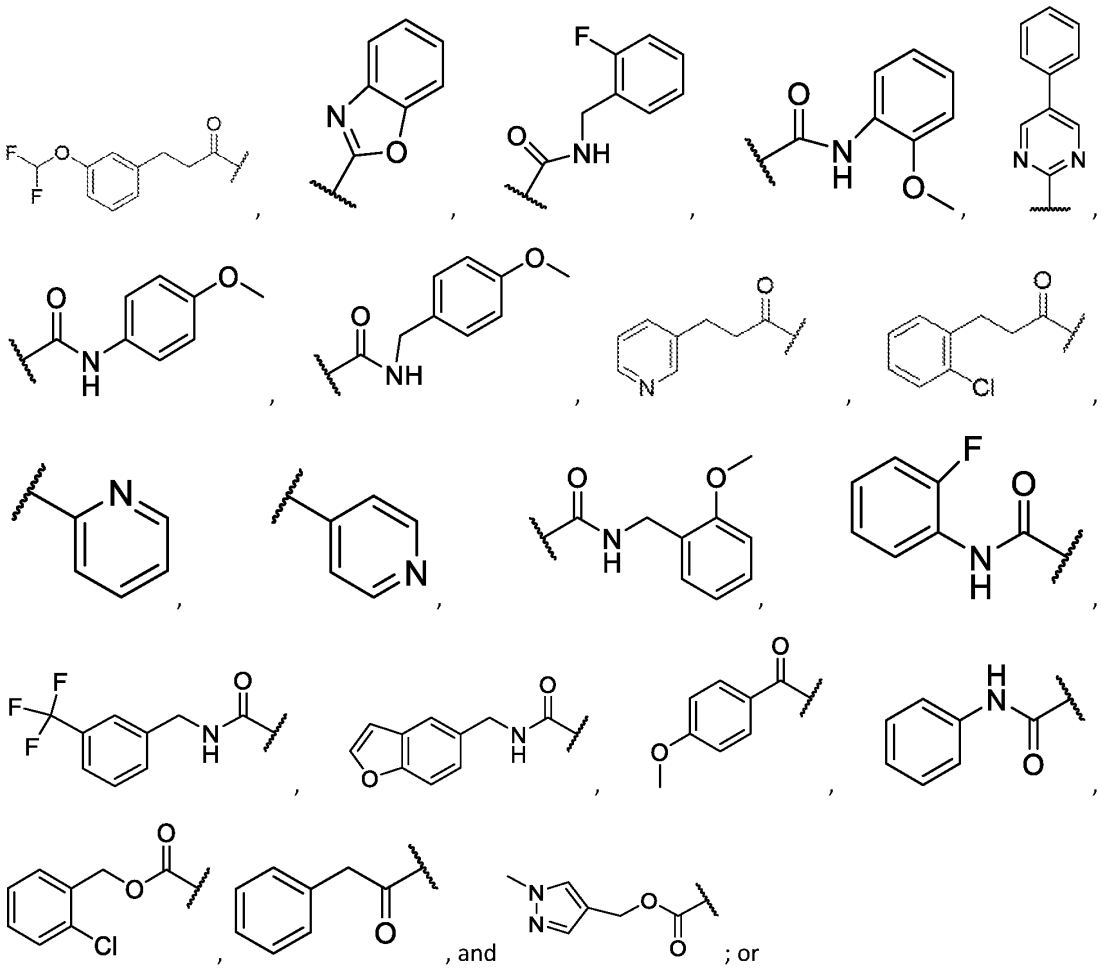
when -V-Z- is absent:

U is absent, CH_2 or $-CH_2CH_2-$.

Preferably, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$, wherein R18 is selected from:





when -V-Z- is absent:

U is absent, CH_2 or $-CH_2CH_2-$.

Preferably, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or

when -V-Z- is absent:

U is absent, CH_2 or $-CH_2CH_2-$.

Preferably, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or

when -V-Z- is absent:

U is absent, CH_2 or $-CH_2CH_2-$.

More preferably, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$,

$-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or

when -V-Z- is absent:

U is absent, CH_2 or $-CH_2CH_2-$.

Preferably, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-N(COCH_3)-CH_2$,

$-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or

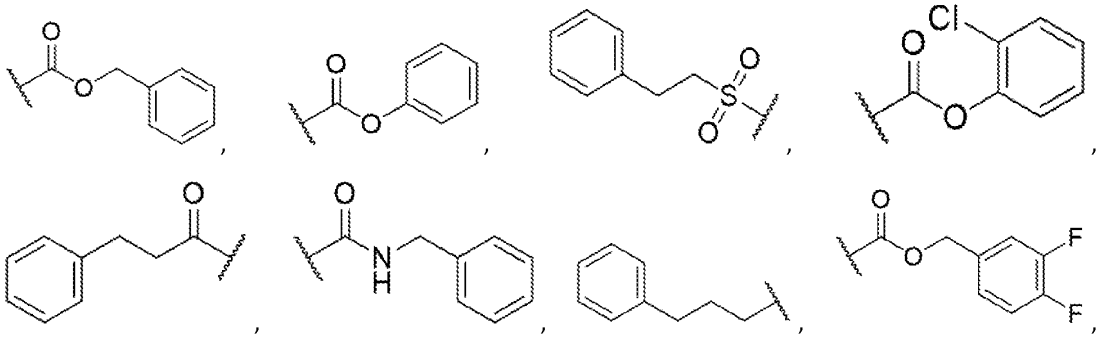
when -V-Z- is absent:

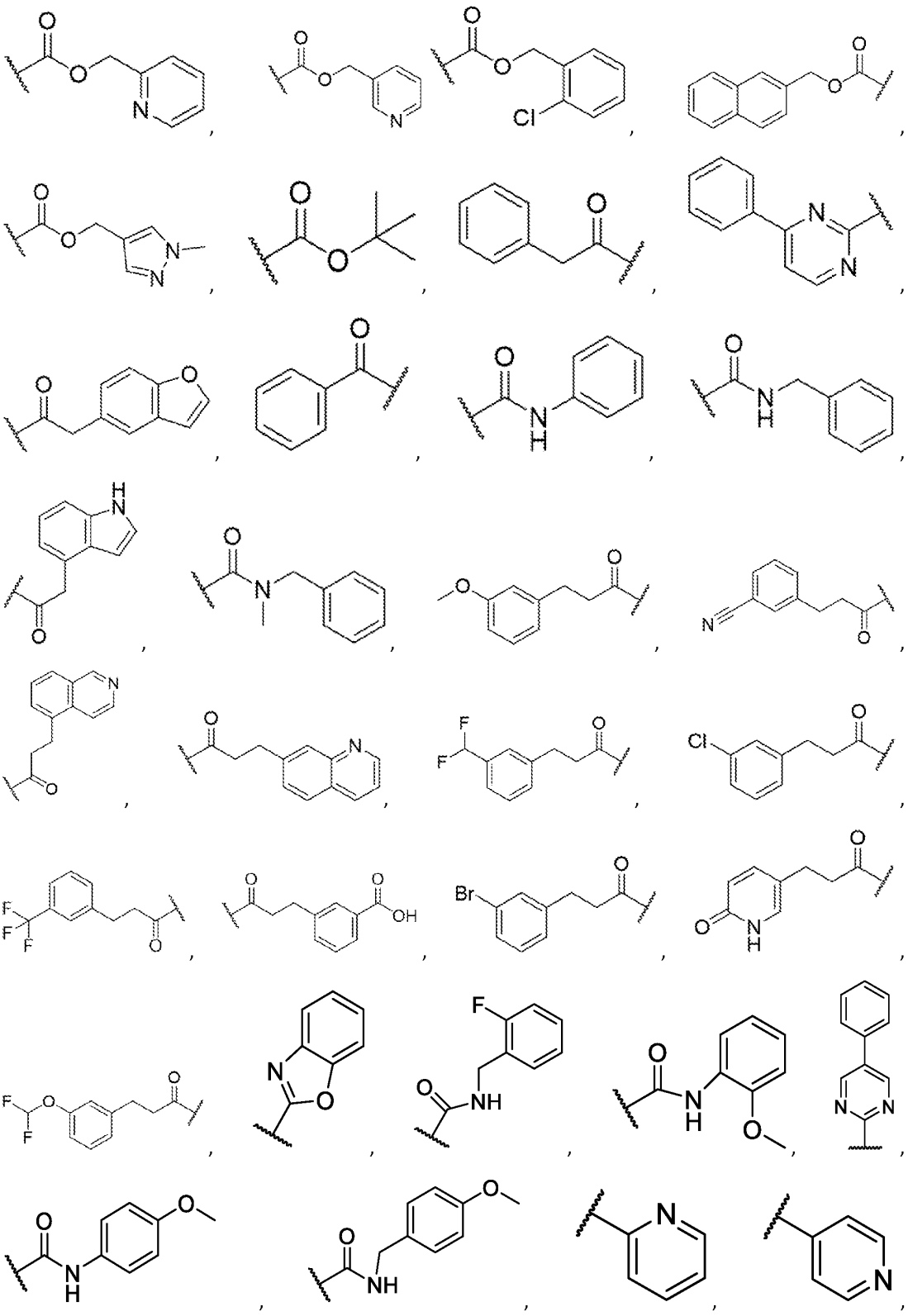
U is absent, CH_2 or $-CH_2CH_2-$.

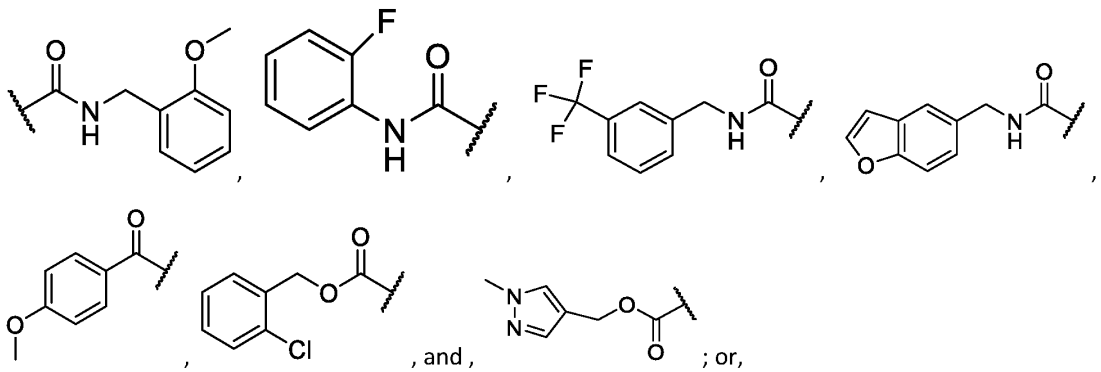
More preferably, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$,

$-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-CH_2-CH_2-O-$,$-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$, wherein R18 is selected from:







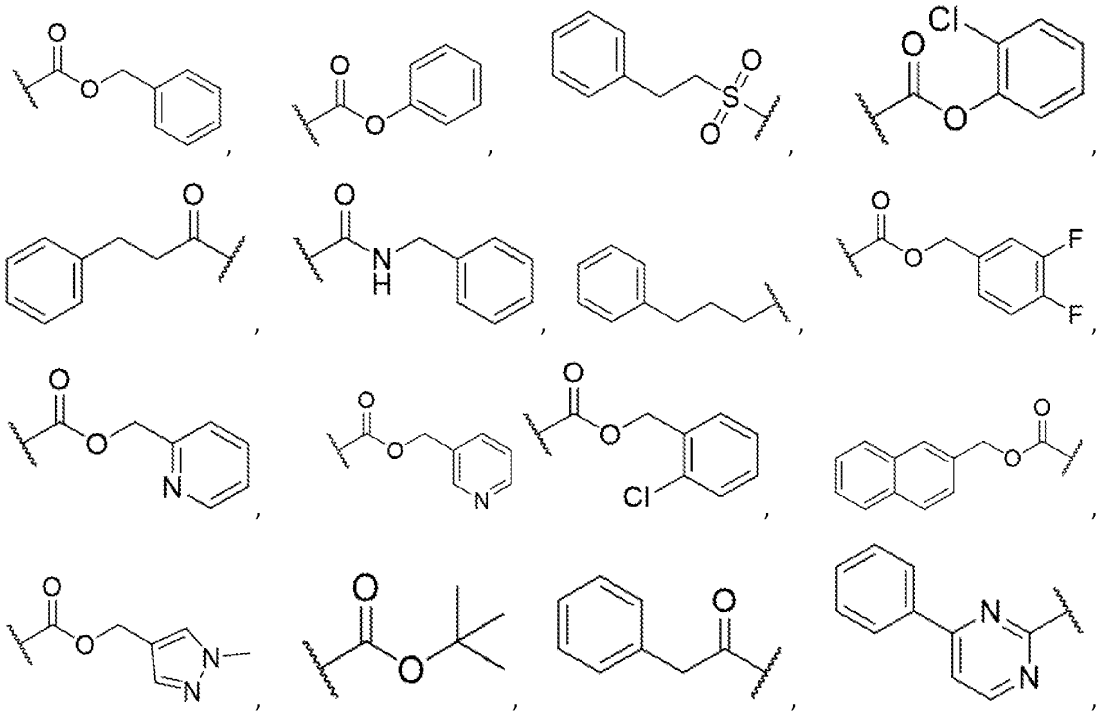
when -V-Z- is absent:

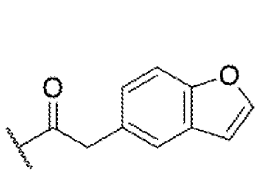
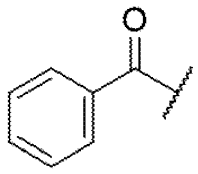
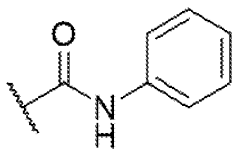
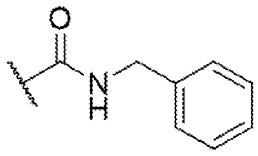
U is absent, CH_2 or $-CH_2CH_2-$.

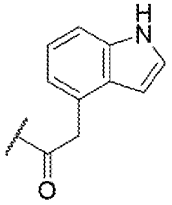
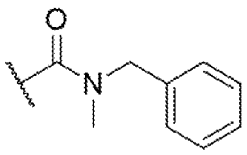
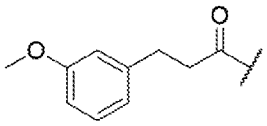
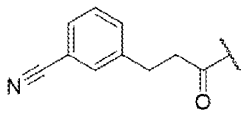
Preferably, when not absent, -V-Z- is selected from:

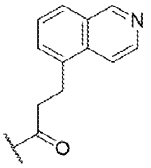
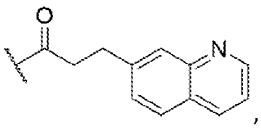
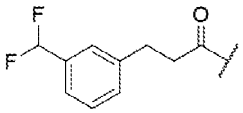
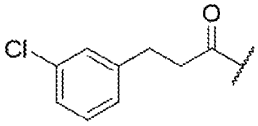
$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-N(COCH_3)-CH_2$,

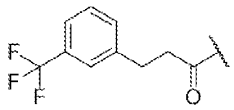
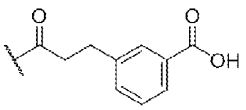
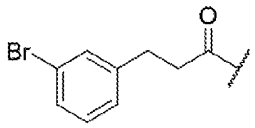
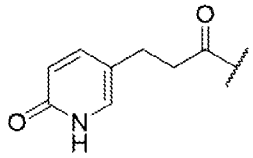
$-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from:

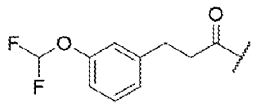
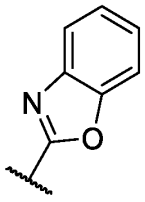
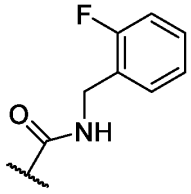
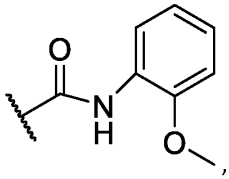
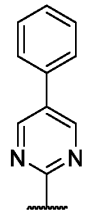


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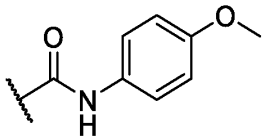
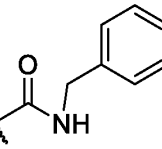
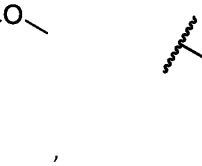
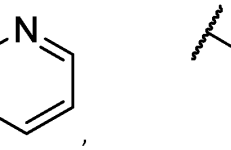
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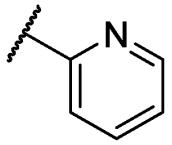
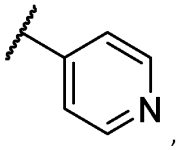
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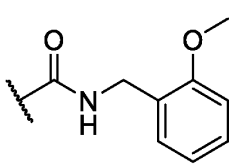
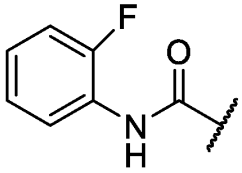
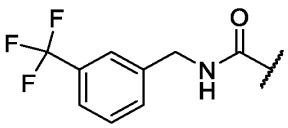
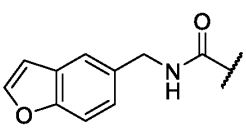
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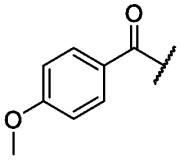
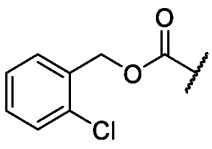
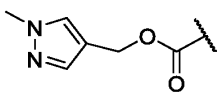
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 ,  , , and  ; or

wherein when -V-Z- is absent:

U is absent, CH_2 or $-CH_2CH_2-$.

More preferably, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or,

when -V-Z- is absent:

U is absent, CH_2 or $-CH_2CH_2-$.

Yet more preferably, -V-Z- is selected from $-CH_2-$, $-O-CH_2-$, $-CH_2-O-$, $-CH_2-CH_2-O-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from:

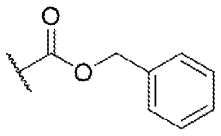
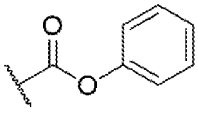
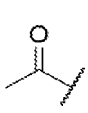
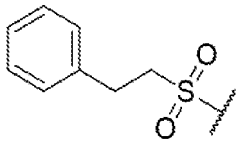
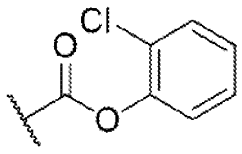
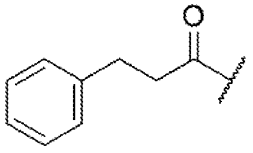
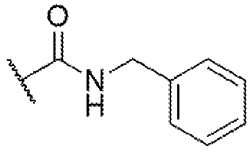
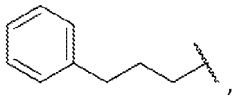
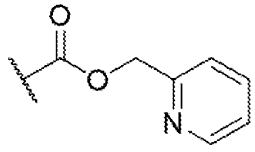
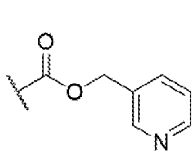
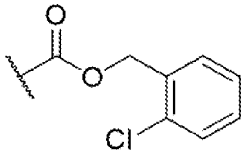
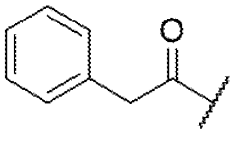
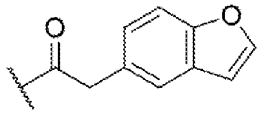
$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

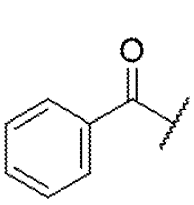
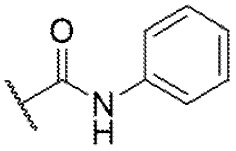
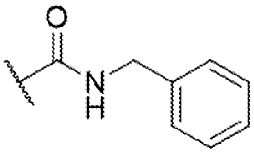
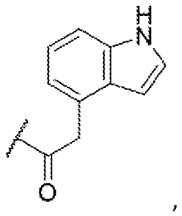
wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or

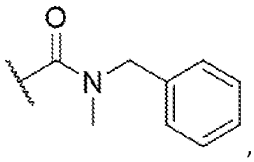
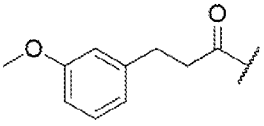
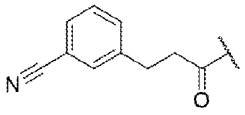
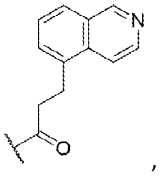
when -V-Z- is absent:

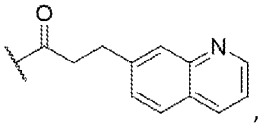
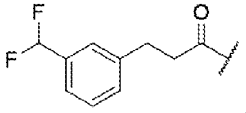
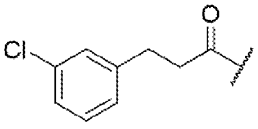
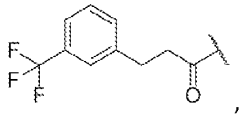
U is absent, CH_2 or $-CH_2CH_2-$.

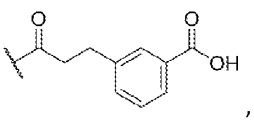
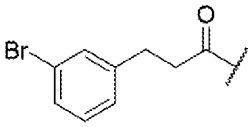
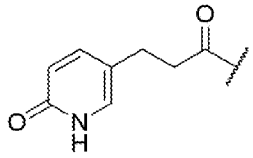
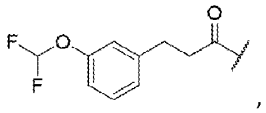
Yet more preferably, -V-Z- is selected from $-CH_2-$, $-O-CH_2-$, $-CH_2-O-$, $-CH_2-CH_2-O-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from:

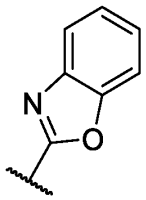
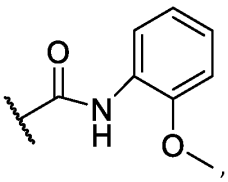
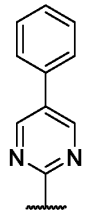
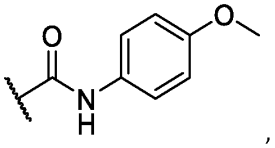
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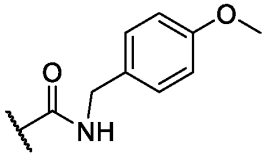
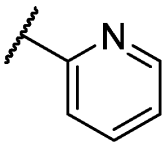
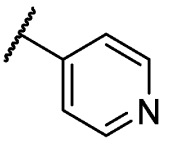
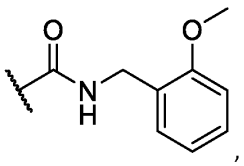
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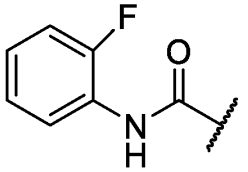
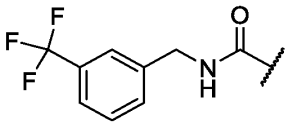
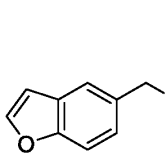
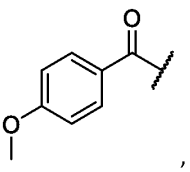
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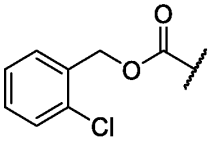
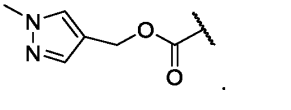
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Yet more preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

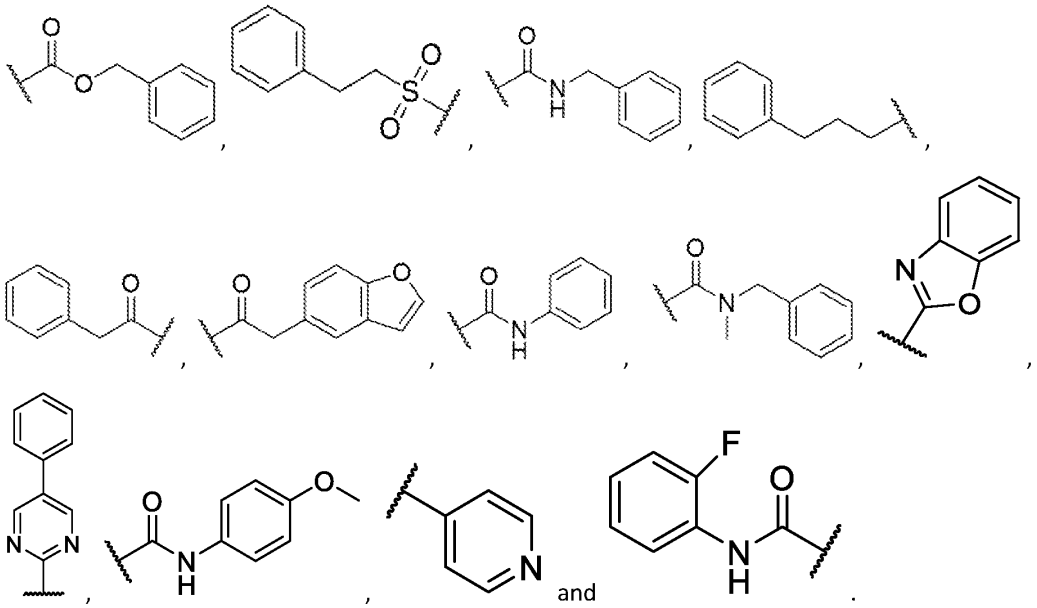
$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or

when -V-Z- is absent:

U is absent, CH_2 or -CH_2CH_2-.

Yet more preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



Yet more preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-.

More preferably, -V-Z- is selected from -O-CH_2- and -CH_2-O-.

More specifically, the invention provides compounds of formula (I) wherein U is absent;

X and Y are independently selected from O, CR1R2, C=O and NR12;

wherein when one of X or Y is C=O, the other is O, CR1R2 or NR12;

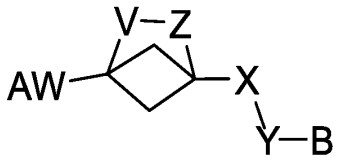
wherein when one of X or Y is NR12, the other is CR1R2 or C=O;

wherein when one of X or Y is O, the other is CR1R2 or C=O;

-V-Z- is -CH_2- or;

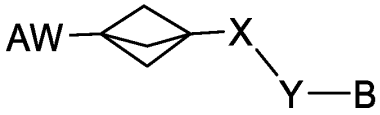
V is O and Z is CR16R17;

which are compounds of formula (1d)



Formula (1d)

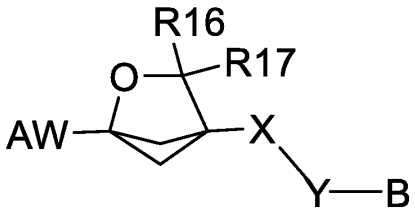
Yet more specifically, the invention provides compounds of formula (I) wherein U is absent and -V-Z- is -CH_2-, which are compounds of formula (1e)



Formula (1e),

and tautomers, isomers, stereoisomers (including enantiomers, diastereoisomers and racemic and scalemic mixtures thereof), deuterated isotopes, and pharmaceutically acceptable salts and/or solvates thereof.

Alternatively, the invention provides compounds of formula (I) wherein U is absent, V is O and Z is CR16R17 which are compounds of formula (1f)



Formula (1f),

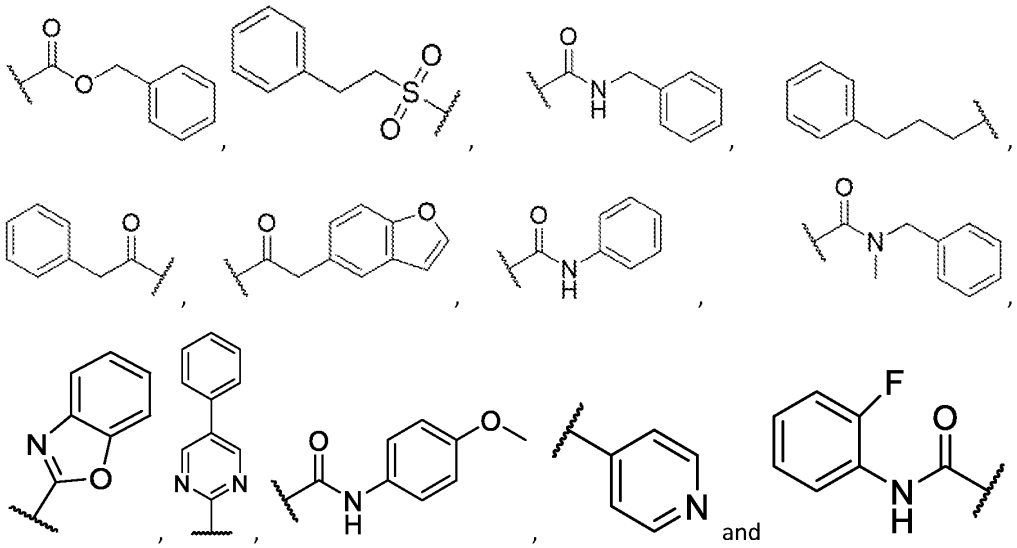
and tautomers, isomers, stereoisomers (including enantiomers, diastereoisomers and racemic and scalemic mixtures thereof), deuterated isotopes, and pharmaceutically acceptable salts and/or solvates thereof.

Preferably, R16 and R17 are both H, or R 16 and R17 are both –CH_3. More preferably, R16 and R17 are both H.

X can be as defined above. In particular, X can be selected from a bond and CR1R2. Preferably, X can be selected from a bond and CH_2. Preferably X is CR1R2. More preferably, X is CH_2.

Y can be as defined above. In particular, Y can be, where possible, selected from O, CR1R2, N and NR12. Preferably Y is, where possible, selected from O, CH_2, N and NH.

Preferably, -V-Z- is -CH_2-, X is CH_2 and Y is NH; -V-Z- is -O-CH_2-, X is CH_2 and Y is NH; -V-Z- is -CH_2-O-, X is CH_2 and Y is NH; -V-Z- is -CH_2-CH_2-O-, X is CH_2 and Y is NH; or -V-Z- is -CH_2-N(R18)-, X is CH_2 and Y is NH; or V-Z- is -N(R18)-CH_2-, X is CH_2 and Y is NH; wherein R18 is selected from:



and

.

Preferably, -V-Z- is -CH_2-, X is CH_2 and Y is NH; -V-Z- is -O-CH_2-, X is CH_2 and Y is NH; -V-Z- is -CH_2-O-, X is CH_2 and Y is NH; or -V-Z- is -CH_2-CH_2-O-, X is CH_2 and Y is NH.

As noted above, X is selected from a bond, O, CR1R2, C=O and NR12. Y can be, where possible, selected from O, CR1R2, CR1, C=O, N and NR12. When one of X or Y is C=O, the other is, where possible, O, CR1R2, CR1, N or NR12. When X is NR12, Y is, where possible, CR1R2, CR1 or C=O. When Y is, where possible, NR12 or N, X is a bond, CR1R2 or C=O. When X is O, Y is, where possible, CR1R2, CR1 or C=O. When Y, where possible, is O, X is a bond, CR1R2 or C=O. When X is a bond, Y is, where possible, O, N or NR12.

X can be CR1R2. Y can be CR1R2. X and Y can be CR1R2.

R1 can be H. R1 can be alkyl, for example small alkyl such as methyl or ethyl, which can be optionally substituted as for alkyl. R1 can be alkoxy, for example methoxy or ethoxy, which can be optionally substituted as for alkoxy. R1 can be OH. R1 can be halo, for example chloro. R1 can be NR13R14, for example NH_2.

R2 can be H. R2 can be alkyl, for example small alkyl such as methyl or ethyl, which can be optionally substituted as for alkyl. R2 can be alkoxy, for example methoxy or ethoxy, which can be optionally substituted as for alkyl. R2 can be OH. R2 can be halo, for example chloro. R2 can be NR13R14, for example NH_2.

R1 can be H and R2 can be alkyl, for example small alkyl such as methyl or ethyl, which can be optionally substituted as for alkyl. R2 can be alkoxy, for example methoxy or ethoxy, which can be optionally substituted as for alkyl. R2 can be OH. R2 can be halo, for example chloro. R2 can be NR13R14, for example NH_2.

At least one of R1 and R2 can be other than H. At least one of R1 and R2 can be H. Preferably, both R1 and R2 are H.

X can be NR12. Y can be NR12 or N. When X is NR12, Y is, where possible, CR1R2, CR1 or C=O. When Y is, where possible, NR12 or N, X is a bond, CR1R2 or C=O. X can be NR12 and Y can, where possible, be CR1R2 (as defined above). Alternatively, X can be CR1R2 (as defined above) and Y can, where possible, be NR12 or N. X can be NR12 and Y can, where possible, be C=O. Alternatively, Y can, where possible, be NR12 or N and X can be C=O.

R12 can be alkyl, for example small alkyl such as methyl or ethyl, which can be optionally substituted as for alkyl. R12 can be cycloalkyl, for example cyclopropyl, which can be substituted as for cycloalkyl. Preferably, R12 is H.

X can be C=O. Y can, where possible, be C=O. When one of X or Y is C=O, the other is, where possible, O, CR1R2, CR1, N or NR12. X can be C=O and Y can, where possible, be CR1R2 (as defined above). Alternatively, X can be CR1R2 (as defined above) and Y can, where possible, be C=O.

X can be O. Y can, where possible, be O. When X is O, Y is, where possible, CR1R2, CR1 or C=O. When Y, where possible, is O, X is a bond, CR1R2 or C=O. X can be O and Y can, where possible, be CR1R2 (as defined above). Alternatively, X can be CR1R2 (as defined above) and Y can, where possible, be O. X can

be O and Y can, where possible, be C=O. Alternatively, X can be C=O and Y can, where possible, be O. X can be O and Y can, where possible, be CR1. X can be a bond and Y can, where possible, be O.

X can be a bond. When X is a bond, Y is, where possible, O, N or NR12. When X is a bond, Y can be, where possible, O. When X is a bond, Y can be, where possible, N. When X is a bond, Y can be, where possible, NR12. Preferably, when X is a bond, Y is, where possible, N or NR12. More preferably, when X is a bond, Y is, where possible, N or NH.

Preferably X is CH_2, and Y is, where possible, N or NR12.

Preferably X is CH_2, and Y is, where possible, N or NH.

Preferably X is CH_2, Y is NR12, and U is absent.

Preferably X is CH_2 and Y is NH.

Preferably X is CH_2, Y is NH and U is absent.

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$; or,
when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CH_2; and Y is NH or N.

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$; or,
when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CH_2; and Y is NH or N.

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$; wherein R18 is selected from: alkyl, $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), C(=O)SR19 and SO_2R19; or,
when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CH_2; and Y is NH or N.

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$; wherein R18 is selected from: alkyl, $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), C(=O)SR19 and SO_2R19; or,

when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CH_2; and Y is NH or N.

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or,

when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CH_2; and Y is NH or N.

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or,

when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CH_2; and Y is NH.

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or,

when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CH_2; and Y is NH.

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or,

when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CH_2; and Y is NH or N.

Preferably, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or,

when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CH_2; and Y is NH or N.

Preferably, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from:

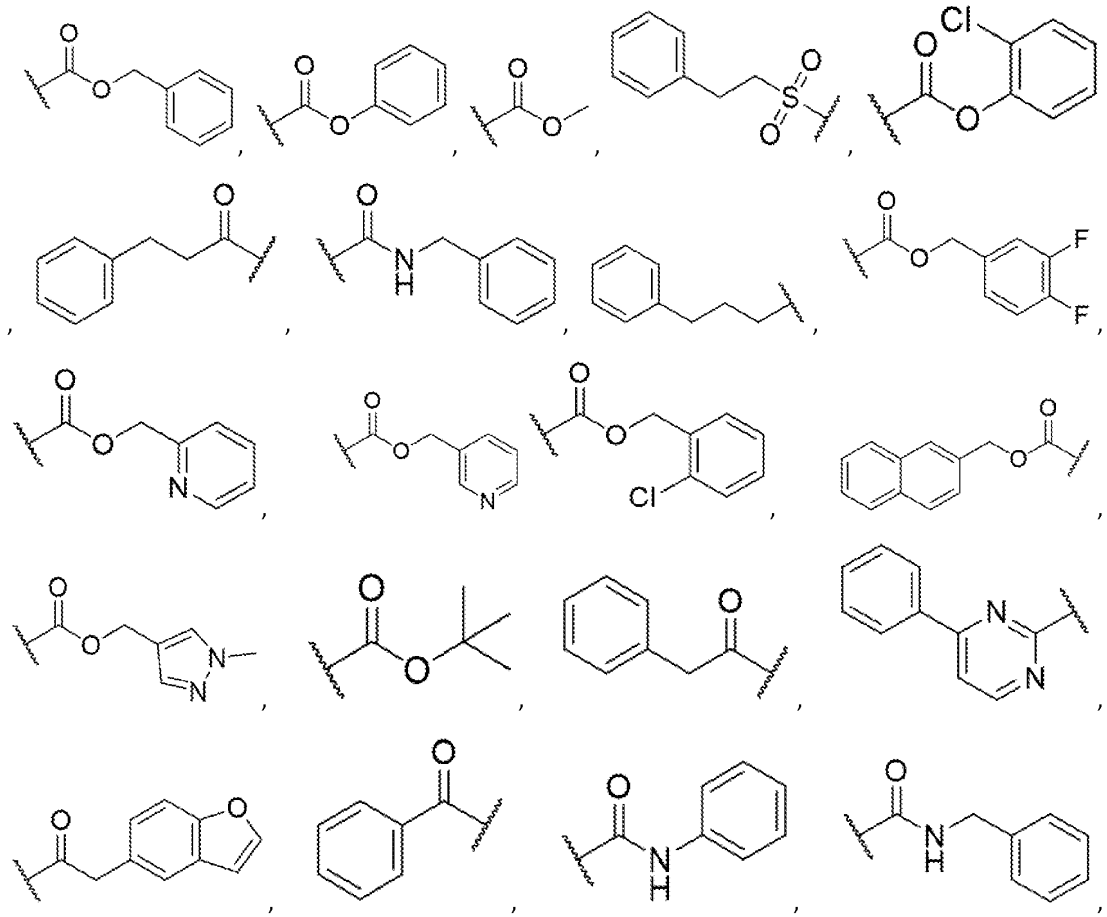
$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

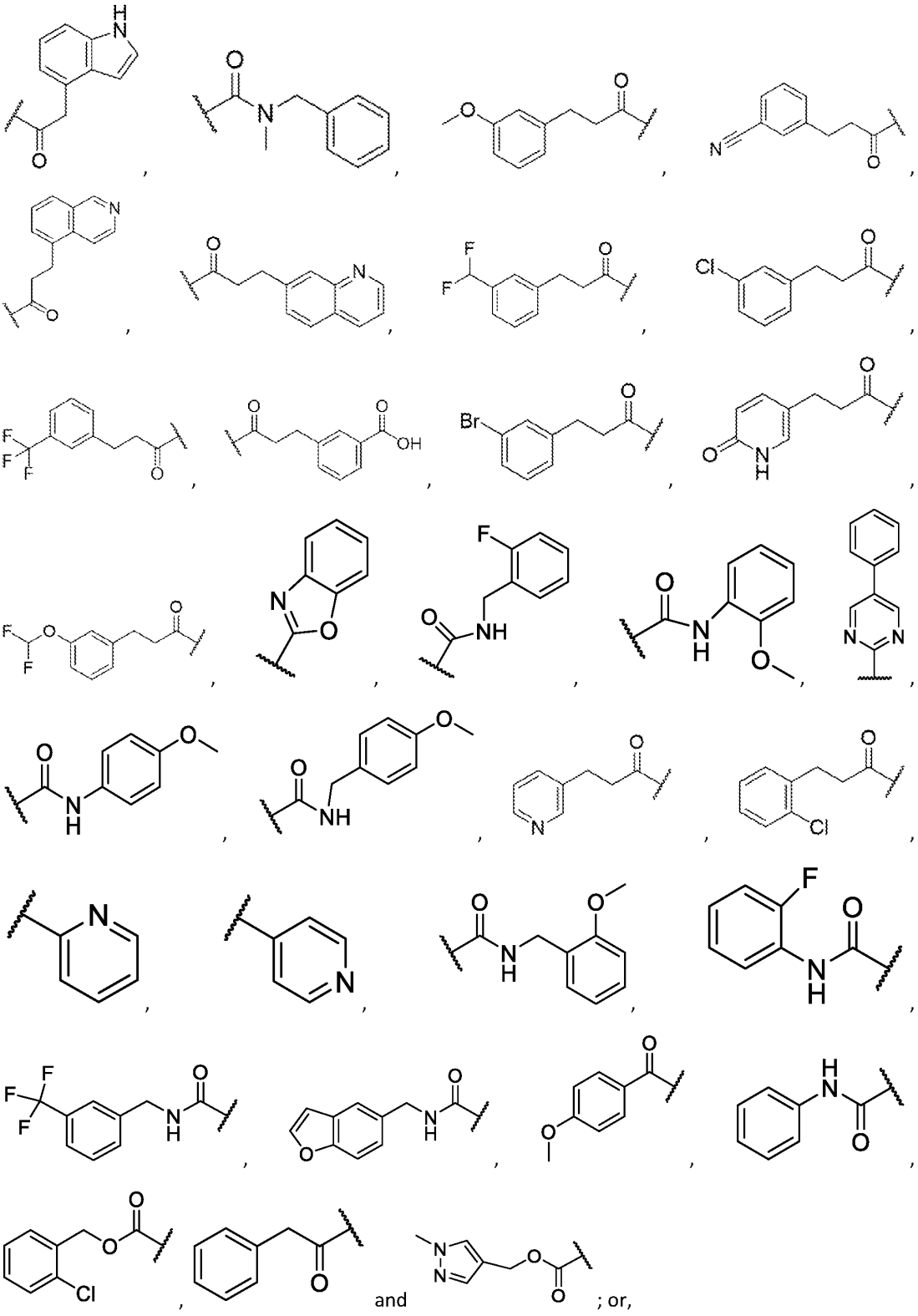
wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or,

when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CH_2; and Y is NH or N.

Preferably, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$, wherein R18 is selected from:

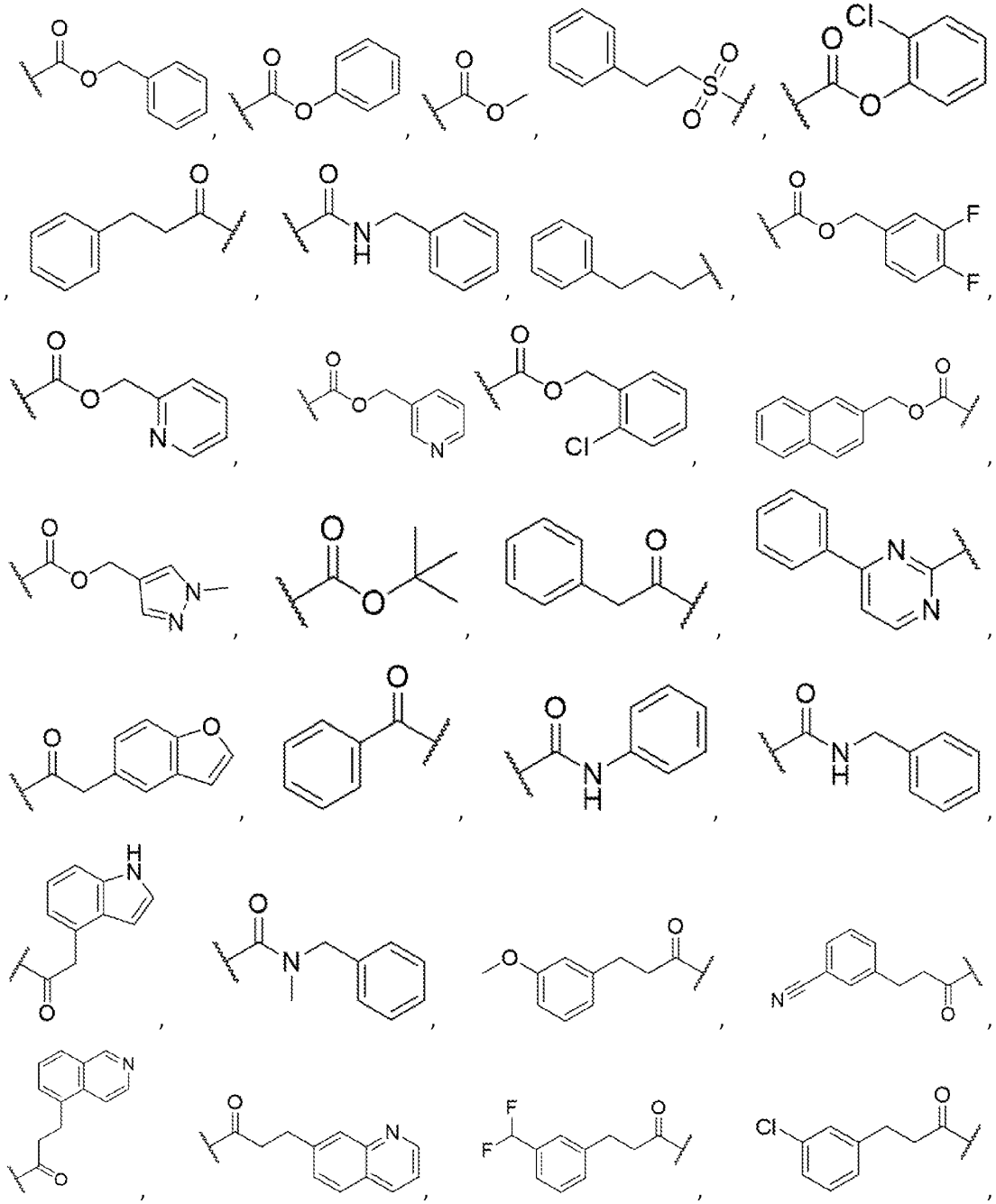


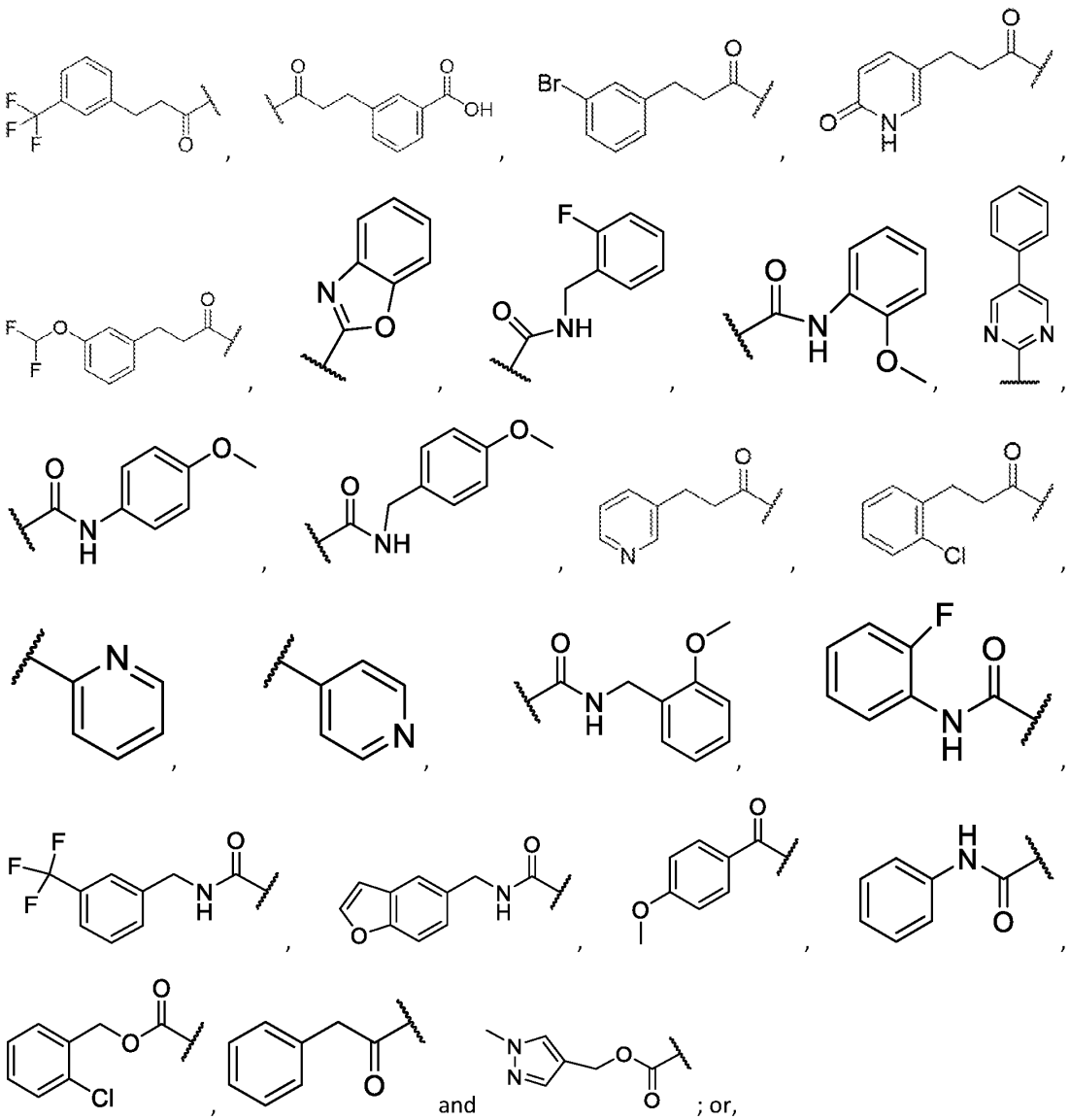


when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CH_2; and Y is NH or N.

Preferably, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$, wherein R18 is selected from:





when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CH_2; and Y is NH or N.

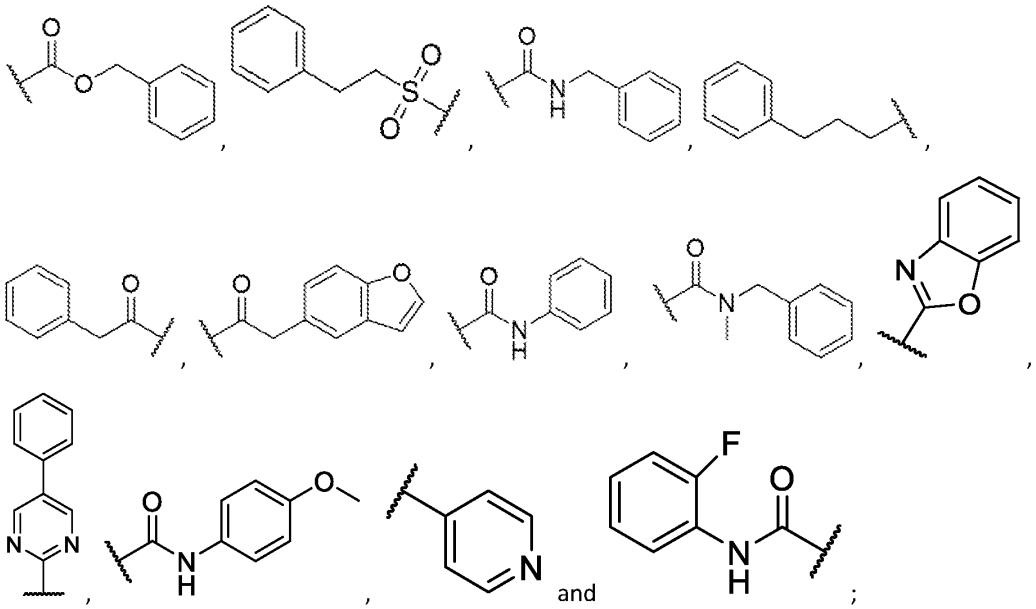
Yet more preferably, -V-Z- is selected from $-CH_2-$, $-O-CH_2-$, $-CH_2-O-$, $-CH_2-CH_2-O-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CH_2; and Y is NH.

Yet more preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



; X is CH_2; and Y is NH.

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CH_2; and Y is NH.

Alternatively, for compounds of formula (1d), X and Y are independently selected from O, CR1R2, C=O and NR12. When one of X or Y is C=O, the other is O, CR1R2 or NR12. When one of X or Y is NH, the other is CR1R2 or C=O. When one of X or Y is O, the other is CR1R2 or C=O.

X can be CR1R2. Y can be CR1R2. X and Y can be CR1R2.

R1 can be H. R1 can be alkyl, for example small alkyl such as methyl or ethyl, which can be optionally substituted as for alkyl. R1 can be alkoxy, for example methoxy or ethoxy, which can be optionally substituted as for alkoxy. R1 can be OH. R1 can be halo, for example chloro. R1 can be NR13R14, for example NH_2.

R2 can be H. R2 can be alkyl, for example small alkyl such as methyl or ethyl, which can be optionally substituted as for alkyl. R2 can be alkoxy, for example methoxy or ethoxy, which can be optionally substituted as for alkyl. R2 can be OH. R2 can be halo, for example chloro. R2 can be NR13R14, for example NH_2.

R1 can be H and R2 can be alkyl, for example small alkyl such as methyl or ethyl, which can be optionally substituted as for alkyl. R2 can be alkoxy, for example methoxy or ethoxy, which can be optionally substituted as for alkyl. R2 can be OH. R2 can be halo, for example chloro. R2 can be NR13R14, for example NH_2.

At least one of R1 and R2 can be other than H. At least one of R1 and R2 can be H. Preferably, both R1 and R2 are H.

X can be NR12. Y can be NR12. When one of X or Y is NR12, the other is CR1R2 or C=O. X can be NR12 and Y can be CR1R2 (as defined above). Alternatively, X can be CR1R2 (as defined above) and Y can be NR12. X can be NR12 and Y can be C=O. Alternatively, Y can be NR12 and X can be C=O.

R12 can be alkyl, for example small alkyl such as methyl or ethyl, which can be optionally substituted as for alkyl. R12 can be cycloalkyl, for example cyclopropyl, which can be substituted as for cycloalkyl. Preferably, R12 is H.

X can be C=O. Y can be C=O. When one of X or Y is C=O, the other is O, CR1R2 or NR12. X can be C=O and Y can be CR1R2 (as defined above). Alternatively, X can be CR1R2 (as defined above) and Y can be C=O.

X can be O. Y can be O. When one of X or Y is O, the other is CR1R2 or C=O. X can be O and Y can be CR1R2 (as defined above). Alternatively, X can be CR1R2 (as defined above) and Y can be O. X can be O and Y can be C=O. Alternatively, X can be C=O and Y can be O.

Preferably, X is CH_2 and Y is NH.

As noted above, B can be selected from:

(i) heteroaryl[a];

(ii) aryl;

(iii) a 5- to 6- membered non-aromatic heterocyclic ring containing one N ring member, which is unsaturated with 1 or 2 double bonds, wherein the non-aromatic heterocyclic ring is optionally substituted by 1, 2 or 3 substituents independently selected from alkyl, alkoxy, aryl[b], OH, OCF_3, halo, oxo, CN, and CF_3; and

(iv) a fused 5,5-, 6,5- or 6,6- bicyclic ring containing an aromatic ring fused to a non-aromatic ring, wherein the bicyclic ring optionally contains one or two N ring members, wherein the fused 5,5-, 6,5- or 6,6- bicyclic ring may be optionally substituted with 1, 2, or 3 substituted by up to three substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, oxo, CN, and CF_3, wherein the 6,5- bicyclic ring may be attached via the 6- or 5- membered ring.

B can be selected from heteroaryl[a] and aryl.

B can be heteroaryl[a] and Y can be attached to B at a carbon atom on the heteroaryl[a] ring.

B can be heteroaryl[a] and Y can be attached to B at a carbon atom on the heteroaryl[a] ring, and the two ring atoms adjacent to the carbon atom on the heteroaryl[a] ring to which Y attaches can both be carbon.

Preferably, B is heteroaryl[a]. When B is heteroaryl[a], B can be substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a]. When B is heteroaryl[a], B can be substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a]. B can be substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

When B is heteroaryl[a], B can be a 5, 6, 9 or 10 membered mono- or bi-cyclic aromatic ring, containing, where possible, 1, 2, 3 or 4 ring members independently selected from N, NR12, S and O; wherein B may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b], -C(=O)OR12, -C(=O)NR13R14 and CF_3. B can be a 5, 6, 9 or 10 membered mono- or bi-cyclic aromatic ring, containing, where possible, 1, 2, 3 or 4 ring members independently selected from N, NR12, S and O; wherein B may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b] and CF_3.

When B is heteroaryl[a], B can be a 9 or 10 membered bi-cyclic aromatic ring, containing, where possible, 1, 2, 3 or 4 ring members independently selected from N, NR12, S and O, optionally substituted as for heteroaryl[a]. B can be a 9 or 10 membered bi-cyclic aromatic ring, containing, where possible, 1, 2, 3 or 4 ring members independently selected from N, NR12, S and O, wherein B may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b], -C(=O)OR12, -C(=O)NR13R14 and CF_3. B can be a 9 or 10 membered bi-cyclic aromatic ring, containing, where possible, 1, 2, 3 or 4 ring members independently selected from N, NR12,

S and O, wherein B may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b] and CF_3.

When B is heteroaryl[a], B can be a 9 or 10 membered bi-cyclic aromatic ring, containing, where possible, 1 or 2 ring members independently selected from N, NR12, S and O, optionally substituted as for heteroaryl[a]. B can be a 9 or 10 membered bi-cyclic aromatic ring, containing, where possible, 1 or 2 ring members independently selected from N, NR12, S and O, wherein B may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b], -C(=O)OR12, -C(=O)NR13R14 and CF_3. B can be a 9 or 10 membered bi-cyclic aromatic ring, containing, where possible, 1 or 2 ring members independently selected from N, NR12, S and O, wherein B may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b] and CF_3.

When B is heteroaryl[a], B can be a 9 or 10 membered bi-cyclic aromatic ring, containing, where possible, 1 or 2 ring members independently selected from N and NR12, optionally substituted as for heteroaryl[a]. B can be a 9 or 10 membered bi-cyclic aromatic ring, containing, where possible, 1 or 2 ring members independently selected from N and NR12, wherein B may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b], -C(=O)OR12, -C(=O)NR13R14 and CF_3. B can be a 9 or 10 membered bi-cyclic aromatic ring, containing, where possible, 1 or 2 ring members independently selected from N and NR12, wherein B may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b] and CF_3.

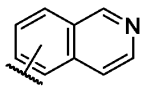
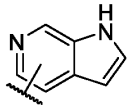
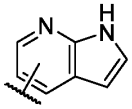
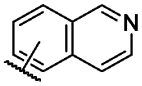
When B is heteroaryl[a], B is preferably isoquinolinyl or azaindole, optionally substituted as for heteroaryl[a]. B is preferably isoquinolinyl or azaindole, optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b], -C(=O)OR12, -C(=O)NR13R14 and CF_3. B is preferably isoquinolinyl or azaindole, optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b] and CF_3. B is preferably isoquinolinyl or azaindole, optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, halo, and $-(CH_2)_{0-3}$-NR13R14.

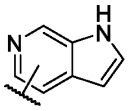
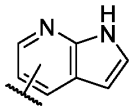
When B is heteroaryl[a], B is preferably isoquinolinyl or azaindole (specifically 7-azaindole), optionally substituted as for heteroaryl[a]. B is preferably isoquinolinyl or azaindole (specifically 7-azaindole), optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b], -C(=O)OR12, -C(=O)NR13R14 and CF_3. B is preferably

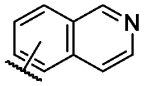
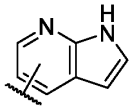
isoquinolinyl or azaindole (specifically 7-azaindole), optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b] and CF_3.

When B is heteroaryl[a], B is preferably isoquinolinyl substituted with $-(CH_2)_{0-3}$-NR13R14 or azaindole optionally substituted as for heteroaryl[a]. B is preferably isoquinolinyl substituted with -NR13R14 or azaindole optionally substituted as for heteroaryl[a]. B is preferably isoquinolinyl substituted with $-NH_2$ or azaindole optionally substituted as for heteroaryl[a]. B is preferably isoquinolinyl substituted with $-NH_2$ or azaindole optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b], -C(=O)OR12, -C(=O)NR13R14 and CF_3. B is preferably isoquinolinyl substituted with $-NH_2$ or azaindole optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b] and CF_3. B is preferably isoquinolinyl substituted with $-NH_2$ or azaindole optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b] and CF_3.

When B is heteroaryl[a], B is preferably isoquinolinyl substituted with $-(CH_2)_{0-3}$-NR13R14 or azaindole (specifically 7-azaindole) optionally substituted as for heteroaryl[a]. B is preferably isoquinolinyl substituted with -NR13R14 or 7-azaindole optionally heteroaryl[a]. B is preferably isoquinolinyl substituted with $-NH_2$ or azaindole (specifically 7-azaindole) optionally substituted as for heteroaryl[a]. B is preferably isoquinolinyl substituted with $-NH_2$ or azaindole (specifically 7-azaindole) optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b], -C(=O)OR12, -C(=O)NR13R14 and CF_3. B is preferably isoquinolinyl substituted with $-NH_2$ or azaindole (specifically 7-azaindole) optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b] and CF_3.

When B is heteroaryl[a], B can be selected from isoquinolinyl  , optionally substituted as for heteroaryl[a]; 6-azaindolyl  , optionally substituted as for heteroaryl[a]; and 7-azaindolyl  , optionally substituted as for heteroaryl[a]. B can be isoquinolinyl  , optionally

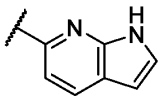
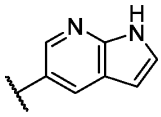
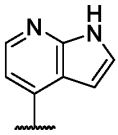
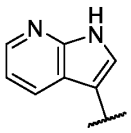
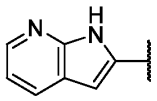
substituted as for heteroaryl[a]. B can be 6-azaindolyl  , optionally substituted as for heteroaryl[a]. B can be 7-azaindolyl  , optionally substituted as for heteroaryl[a].

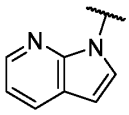
When B is heteroaryl[a], B is preferably selected from isoquinolinyl  , optionally substituted as for heteroaryl[a]; and 7-azaindolyl  , optionally substituted as for heteroaryl[a].

When B is heteroaryl[a], B is preferably isoquinolinyl or azaindole, wherein Y is attached to B at a carbon atom on the heteroaryl[a] ring. When B is heteroaryl[a], B is preferably isoquinolinyl or azaindole, wherein Y is attached to B at a carbon atom on the heteroaryl[a] ring, and the two ring atoms adjacent to the carbon atom on the heteroaryl[a] ring to which Y attaches are both carbon.

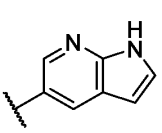
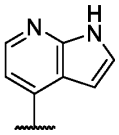
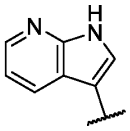
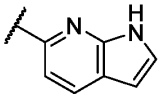
When B is heteroaryl[a], B is preferably isoquinolinyl or azaindole (specifically 7-azaindole), wherein Y is attached to B at a carbon atom on the heteroaryl[a] ring. When B is heteroaryl[a], B is preferably isoquinolinyl or azaindole, wherein Y is attached to B at a carbon atom on the heteroaryl[a] ring, and the two ring atoms adjacent to the carbon atom on the heteroaryl[a] ring to which Y attaches are both carbon.

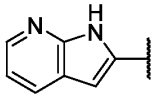
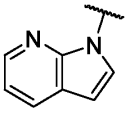
It will be understood that, in the instance when Y is attached to B at a carbon atom on the heteroaryl[a] ring, the attachment of Y to B can be at any carbon on the heteroaryl[a] ring, so long as the remainder of the ring is still a heteroaryl ring. For example, if B is 7-azaindole, the attachment to Y can be at any of

the following ring atoms:  ,  ,  ,  or  ,

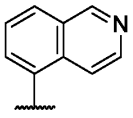
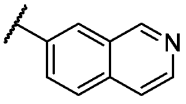
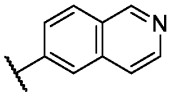
but not at a nitrogen ring atom:  .

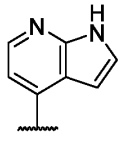
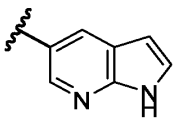
It will be understood that, in the instance when Y is attached to B at a carbon atom on the heteroaryl[a] ring, and the two ring atoms adjacent to the carbon atom on the heteroaryl[a] ring to which Y attaches are both carbon, these adjacent ring atoms can be, where possible, substituted or unsubstituted as defined in the embodiment or claim. Further, for example, if B is 7-azaindole, the attachment to Y can be at any of the following ring atoms:

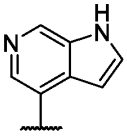
 ,  or  , but not at the following ring atoms:  ,

 or  .

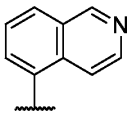
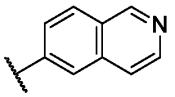
B can be selected from:

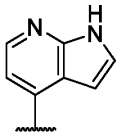
isoquinolinyl, selected from  ,  and  , optionally substituted as for heteroaryl[a];

7-azaindolyl  and  , optionally substituted as for heteroaryl[a]; and

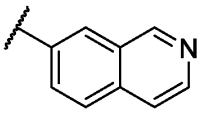
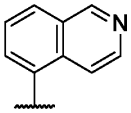
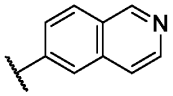
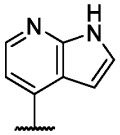
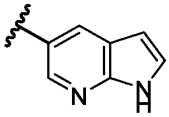
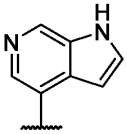
6-azaindolyl  , optionally substituted as for heteroaryl[a].

B can preferably be selected from:

isoquinolinyl, selected from  and  , optionally substituted as for heteroaryl[a]; and

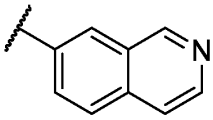
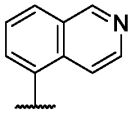
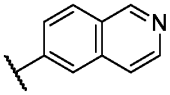
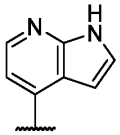
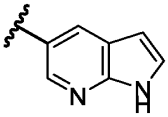
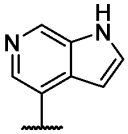
7-azaindolyl  optionally substituted as for heteroaryl[a].

When B is isoquinolinyl or azaindole, B can be selected from

 ,  ,  ,  ,  , and  ,

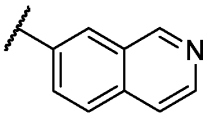
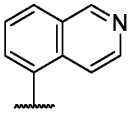
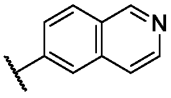
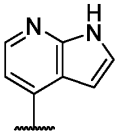
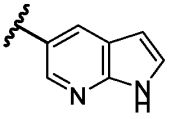
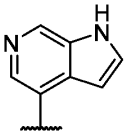
optionally substituted as for heteroaryl[a].

When B is isoquinolinyl or azaindole, B is preferably selected from

 ,  ,  ,  ,  , and  ,

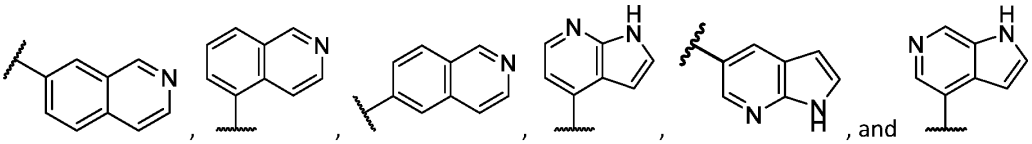
optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b] and CF_3.

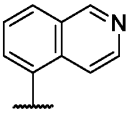
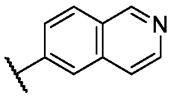
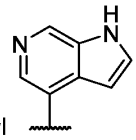
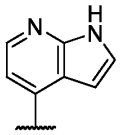
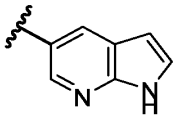
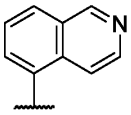
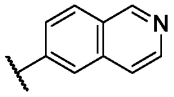
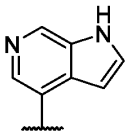
When B is isoquinolinyl or azaindole, B is preferably selected from

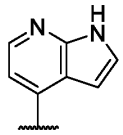
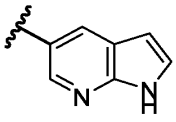
 ,  ,  ,  ,  , and  ,

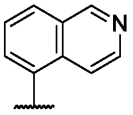
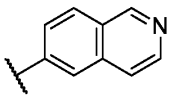
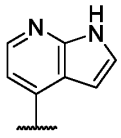
optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, halo, and $-(CH_2)_{0-3}$-NR13R14.

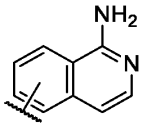
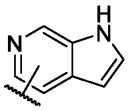
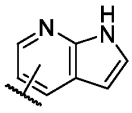
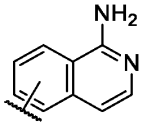
When B is isoquinolinyl or azaindole, B is preferably selected from

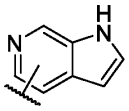
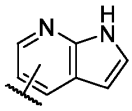

, optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, halo, and -NH_2.

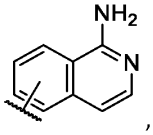
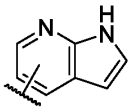
More specifically, B is selected from isoquinolinyl, selected from  and  , substituted with NH_2, optionally further substituted with 1 or 2 substituents as for heteroaryl[a]; 6-azaindolyl  , optionally substituted as for heteroaryl[a]; and 7-azaindolyl selected from  and  , optionally substituted as for heteroaryl[a]. B can be isoquinolinyl, selected from  and  , substituted with NH_2, optionally further substituted with 1 or 2 substituents as for heteroaryl[a]. B can be 6-azaindolyl  , optionally substituted as

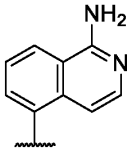
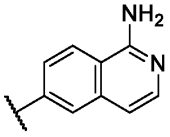
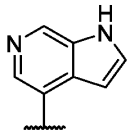
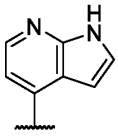
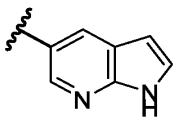
for heteroaryl[a]. B can be 7-azaindolyl selected from  and  , optionally substituted as for heteroaryl[a].

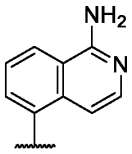
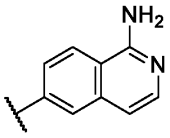
More specifically, B is selected from isoquinolinyl, selected from  and  , substituted with NH_2, optionally further substituted with 1 or 2 substituents as for heteroaryl[a]; and 7-azaindolyl  , optionally substituted as for heteroaryl[a].

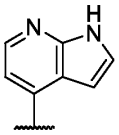
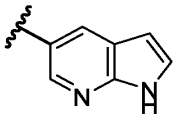
Yet more specifically, B is selected from: isoquinolinyl, substituted with NH_2 at the 1- position  , optionally further substituted with 1 or 2 substituents as for heteroaryl[a]; 6-azaindolyl  , optionally substituted as for heteroaryl[a]; and 7-azaindolyl  , optionally substituted as for heteroaryl[a]. B can be isoquinolinyl, substituted with NH_2 at the 1- position  , optionally further substituted with 1 or 2 substituents as for heteroaryl[a]. B can be 6-

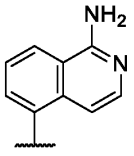
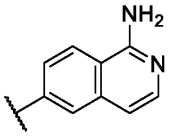
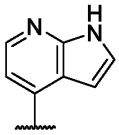
azaindolyl  , optionally substituted as for heteroaryl[a]. B can be 7-azaindolyl  , optionally substituted as for heteroaryl[a].

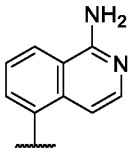
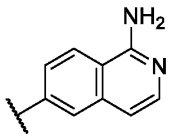
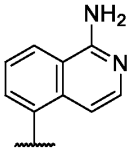
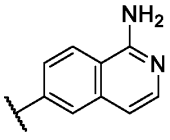
Yet more specifically, B is selected from: isoquinolinyl, substituted with NH_2 at the 1- position  , optionally further substituted with 1 or 2 substituents as for heteroaryl[a]; and 7-azaindolyl  , optionally substituted as for heteroaryl[a].

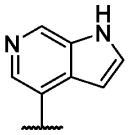
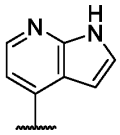
Preferably, when B is heteroaryl[a], B is selected from: isoquinolinyl, substituted with NH_2 at the 1- position, selected from  and  , optionally further substituted with 1 or 2 substituents as for heteroaryl[a]; 6-azaindolyl  , optionally substituted as for heteroaryl[a]; and 7-azaindolyl selected from  and  , optionally substituted as for heteroaryl[a].

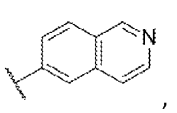
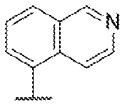
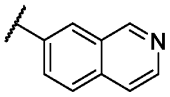
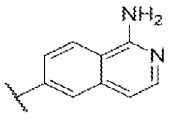
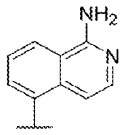
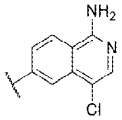
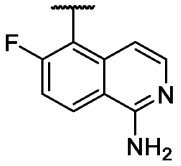
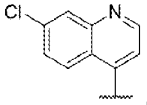
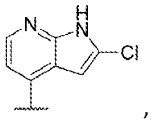
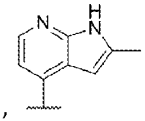
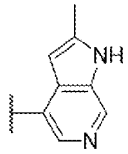
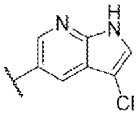
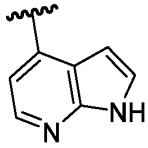
Preferably, when B is heteroaryl[a], B is selected from: isoquinolinyl, substituted with NH_2 at the 1- position, selected from  and  , optionally further substituted with 1 or 2

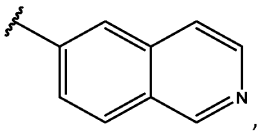
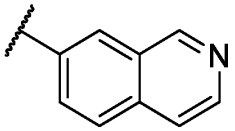
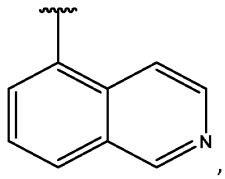
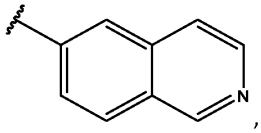
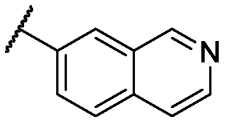
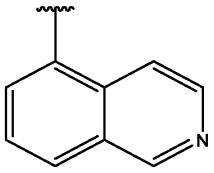
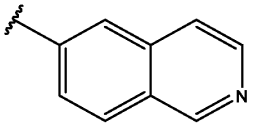
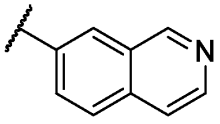
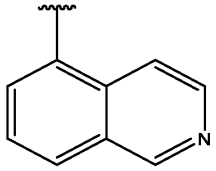
substituents as for heteroaryl[a]; and 7-azaindolyl selected from  and  , optionally substituted as for heteroaryl[a].

Preferably, when B is heteroaryl[a], B is selected from: isoquinolinyl, substituted with NH_2 at the 1- position, selected from  and  , optionally further substituted with 1 or 2 substituents as for heteroaryl[a]; and 7-azaindolyl  , optionally substituted as for heteroaryl[a].

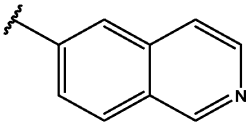
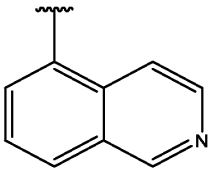
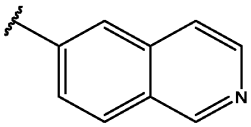
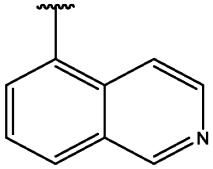
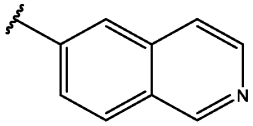
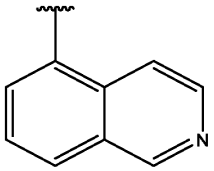
Specifically, B can be isoquinolinyl, substituted with NH_2 at the 1- position, selected from  and  , optionally further substituted with 1 or 2 substituents as for heteroaryl[a]. B can be isoquinolinyl, substituted with NH_2 at the 1- position  , optionally further substituted with 1 or 2 substituents as for heteroaryl[a]. B can be isoquinolinyl, substituted with NH_2 at the 1- position  , optionally further substituted with 1 or 2 substituents as for heteroaryl[a]. B can be

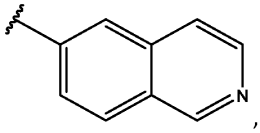
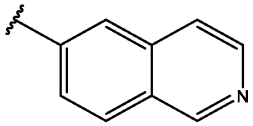
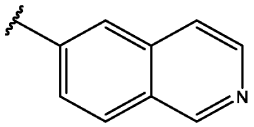
6-azaindolyl  , optionally substituted as for heteroaryl[a]. B can be 7-azaindolyl  , optionally substituted as for heteroaryl[a].

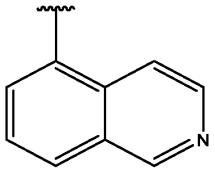
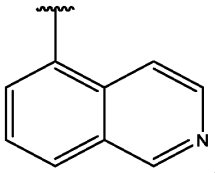
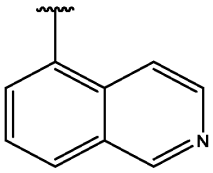
When B is isoquinolinyl or azaindole B can be selected from  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , and  .

When B is isoquinolinyl, B can be selected from  ,  , and  , optionally substituted as for heteroaryl[a]. B can be selected from  ,  , and  , optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b], -C(=O)OR12, -C(=O)NR13R14 and CF_3. B can be selected from  ,  , and  , optionally

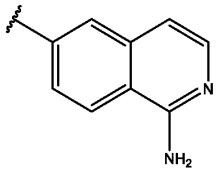
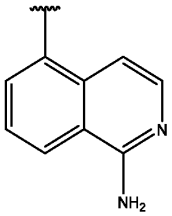
substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, $aryl^b$, $-(CH_2)_{0-3}$-NR13R14, $heteroaryl^b$ and CF_3.

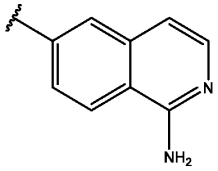
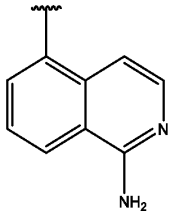
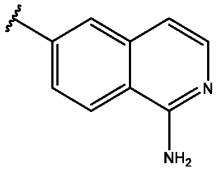
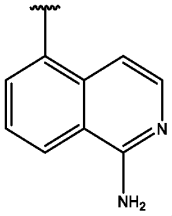
When B is isoquinolinyl, B can be selected from  and  , optionally substituted as for $heteroaryl^a$. B can be selected from  and  , optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, $aryl^b$, $-(CH_2)_{0-3}$-NR13R14, $heteroaryl^b$, -C(=O)OR12, -C(=O)NR13R14 and CF_3. B can be selected from  and  , optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, $aryl^b$, $-(CH_2)_{0-3}$-NR13R14, $heteroaryl^b$ and CF_3.

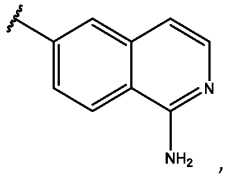
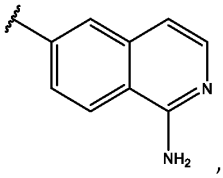
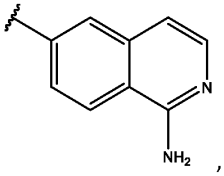
When B is isoquinolinyl, B can be  , optionally substituted as for $heteroaryl^a$. B can be  , optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, $aryl^b$, $-(CH_2)_{0-3}$-NR13R14, $heteroaryl^b$, -C(=O)OR12, -C(=O)NR13R14 and CF_3. B can be  , optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, $aryl^b$, $-(CH_2)_{0-3}$-NR13R14, $heteroaryl^b$ and CF_3.

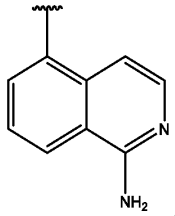
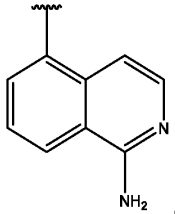
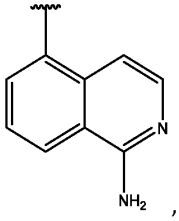
When B is isoquinolinyl, B can be  , optionally substituted as for heteroaryl[a]. B can be  , optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b], -C(=O)OR12, -C(=O)NR13R14 and CF_3. B can be  , optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b] and CF_3.

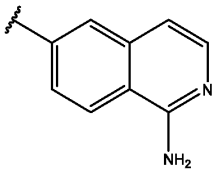
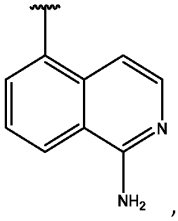
When B is heteroaryl[a], B is preferably isoquinolinyl, substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a]. B is preferably isoquinolinyl, substituted with NH_2, and optionally substituted with 1, or 2 further substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b], -C(=O)OR12, -C(=O)NR13R14 and CF_3. B is preferably isoquinolinyl, substituted with NH_2, and optionally substituted with 1, or 2 further substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b] and CF_3.

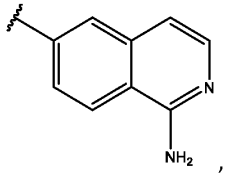
When B is isoquinolinyl, substituted with NH_2, B can be selected from  and  , optionally substituted with 1 or 2 further substituents as for heteroaryl[a]. B can be

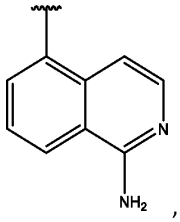
selected from  and  , optionally substituted with 1, or 2 further substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, $aryl^b$, $-(CH_2)_{0-3}$-NR13R14,  $heteroaryl^b$, -C(=O)OR12, -C(=O)NR13R14 and CF_3. B can be selected from  and , optionally substituted with 1, or 2 further substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, $aryl^b$, $-(CH_2)_{0-3}$-NR13R14, $heteroaryl^b$ and CF_3.

When B is isoquinolinyl, substituted with NH_2, B can be  , optionally substituted with 1 or 2 further substituents as for $heteroaryl^a$. B can be  , optionally substituted with 1, or 2 further substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, $aryl^b$, $-(CH_2)_{0-3}$-NR13R14, $heteroaryl^b$, -C(=O)OR12, -C(=O)NR13R14 and CF_3. B can be  , optionally substituted with 1, or 2 further substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, $aryl^b$, $-(CH_2)_{0-3}$-NR13R14, $heteroaryl^b$ and CF_3.

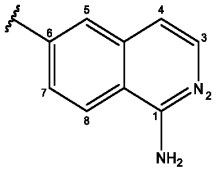
When B is isoquinolinyl, substituted with NH_2, B can be  , optionally substituted with 1 or 2 further substituents as for heteroaryl[a]. B can be  , optionally substituted with 1, or 2 further substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b], -C(=O)OR12, -C(=O)NR13R14 and CF_3. B can be  , optionally substituted with 1, or 2 further substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b] and CF_3.

When B is isoquinolinyl, substituted with NH_2, B can be selected from  and  , optionally substituted with a further substituent selected from halo.

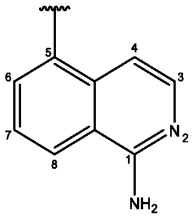
When B is isoquinolinyl, substituted with NH_2, B can be  , optionally substituted with a further substituent selected from halo (e.g. chloro).



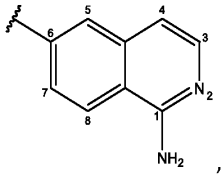
When B is isoquinolinyl, substituted with NH_2, B can be , optionally substituted with a further substituent selected from halo (e.g. chloro).



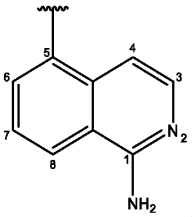
When B isoquinolinyl, substituted with NH_2, B can be selected from and



, optionally substituted with a further substituent selected from halo (e.g. chloro) at the carbon marked as 4.

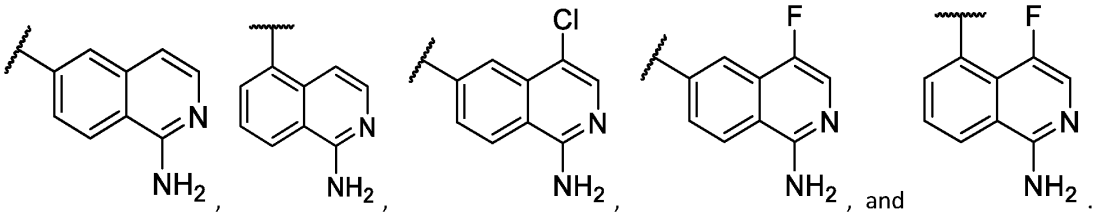


When B is isoquinolinyl, substituted with NH_2, B can be , optionally substituted with a further substituent selected from halo (e.g. chloro) at the carbon marked as 4.

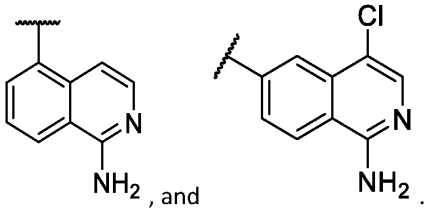


When B is isoquinolinyl, substituted with NH_2, B can be , optionally substituted with a further substituent selected from halo (e.g. chloro), at the carbon marked as 4.

Preferably, B is selected from:



More preferably, B is selected from:



When B is heteroaryl[a], B can be a 5, 6, 9 or 10 membered mono- or bi-cyclic aromatic ring, containing, where possible, 1, 2, 3 or 4 ring members independently selected from N, NR12, S and O which is substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, CN, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b], -C(=O)OR12, -C(=O)NR13R14 and CF_3.

When B is heteroaryl[a], B can be a 9 or 10 membered bi-cyclic aromatic ring, containing, where possible, 1, 2, 3 or 4 ring members independently selected from N, NR12, S and O which is substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, CN, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b], -C(=O)OR12, -C(=O)NR13R14 and CF_3

When B is heteroaryl[a], B can be a 5, 6, 9 or 10 membered mono- or bi-cyclic aromatic ring, containing, where possible, 1, 2, 3 or 4 ring members independently selected from N, NR12, S and O which is substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b], -C(=O)OR12, -C(=O)NR13R14 and CF_3.

When B is heteroaryl[a], B can be a 9 or 10 membered bi-cyclic aromatic ring, containing, where possible, 1, 2, 3 or 4 ring members independently selected from N, NR12, S and O which is substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b], -C(=O)OR12, -C(=O)NR13R14 and CF_3.

When B is heteroaryl[a], B can be a 5, 6, 9 or 10 membered mono- or bi-cyclic aromatic ring, containing, where possible, 1, 2, 3 or 4 ring members independently selected from N, NR12, S and O which is substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b] and CF_3.

When B is heteroaryl[a], B can be a 9 or 10 membered bi-cyclic aromatic ring, containing, where possible, 1, 2, 3 or 4 ring members independently selected from N, NR12, S and O which is substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b] and CF_3.

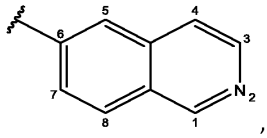
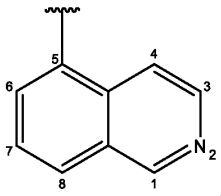
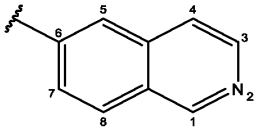
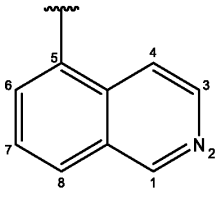
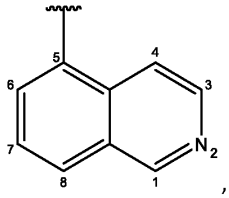
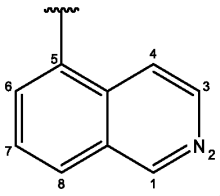
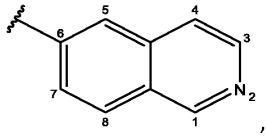
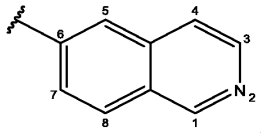
When B is heteroaryl[a], B can be quinolinyl or isoquinolinyl which is substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, CN, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b], -C(=O)OR12, -C(=O)NR13R14 and CF_3. B can be quinolinyl or isoquinolinyl which is substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b], -C(=O)OR12, -C(=O)NR13R14 and CF_3. B can be quinolinyl or isoquinolinyl which is substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b] and CF_3. When B is heteroaryl[a], B can be isoquinolinyl which is substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, CN, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b], -C(=O)OR12, -C(=O)NR13R14 and CF_3. B can be isoquinolinyl which is substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b], -C(=O)OR12, -C(=O)NR13R14 and CF_3. B can be isoquinolinyl which is substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b] and CF_3.

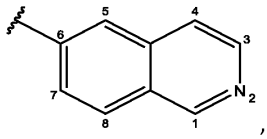
When B is heteroaryl[a], B can be isoquinolinyl, optionally substituted as for heteroaryl[a].

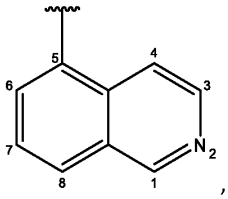
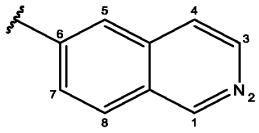
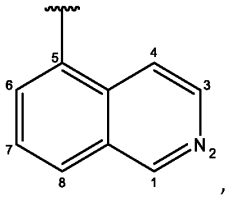
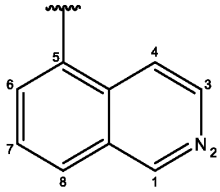
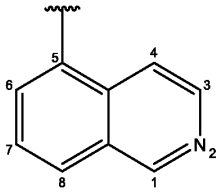
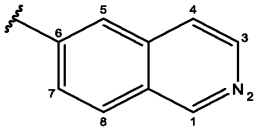
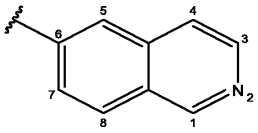
When B is heteroaryl[a], B can be isoquinolinyl substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, CN, aryl[b], $-(CH_2)_{1-3}$-NR13R14, heteroaryl[b], -C(=O)OR12, -C(=O)NR13R14 and CF_3.

When B is heteroaryl[a], B can be isoquinolinyl substituted with 1, 2 or 3 substituents independently selected from alkoxy.

When B is heteroaryl[a], B can be isoquinolinyl substituted with 1, 2 or 3 substituents selected from –OMe.

When B is heteroaryl[a], B can be isoquinolinyl substituted with -OMe. B can be selected from:  , substituted with -OMe at one of the carbons marked as 3, 4, 5, 7 or 8; and  , substituted with -OMe at one of the carbons marked as 3, 4, 6, 7 or 8. B can be selected from  and  , substituted with -OMe at the carbon marked as 8. B can be  , substituted with -OMe at one of the carbons marked as 3, 4, 6, 7 or 8. B can be  , substituted with -OMe at the carbon marked as 8. B can be  , substituted with -OMe at one of the carbons marked as 3, 4, 5, 7 or 8. B can be  , substituted with -OMe at the carbon marked as 8.

When B is heteroaryl[a], B can be isoquinolinyl substituted with -Me. B can be selected from:  , substituted with -Me at one of the carbons marked as 3, 4, 5, 7 or 8; and

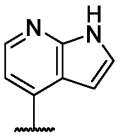
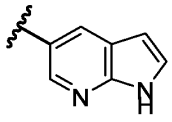
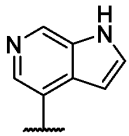

, substituted with -Me at one of the carbons marked as 3, 4, 6, 7 or 8. B can be selected from  and  , substituted with -Me at the carbon marked as 8. B can be  , substituted with -Me at one of the carbons marked as 3, 4, 6, 7 or 8. B can be  , substituted with -Me at the carbon marked as 8. B can be  , substituted with -Me at one of the carbons marked as 3, 4, 5, 7 or 8. B can be  , substituted with -Me at the carbon marked as 8.

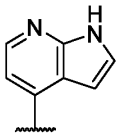
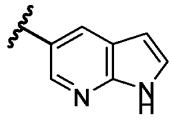
When B is heteroaryl[a], B can be a 9-membered, bi-cyclic aromatic ring containing 1 or 2 ring members independently selected from N, NR12, S and O; wherein B may be optionally substituted as for heteroaryl[a].

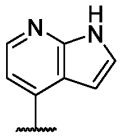
When B is heteroaryl[a], B can be a 9-membered, bi-cyclic aromatic ring containing 1 or 2 ring members independently selected from N, NR12, S and O; wherein B is substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, CN, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b], -C(=O)OR12, -C(=O)NR13R14 and CF_3; wherein the substituents on B are attached to carbon ring members only.

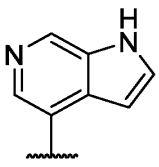
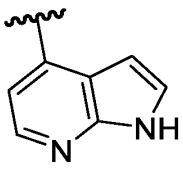
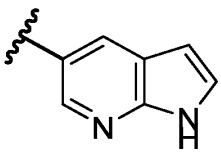
As noted above, B can preferably be azaindole, optionally substituted as for heteroaryl[a]. Specifically, B can be selected from 4-azaindole, 5-azaindole, 6-azaindole and 7-azaindole, each optionally substituted as for heteroaryl[a]. Preferably, B is 7-azaindole.

B can be 7-azaindole optionally substituted as for heteroaryl[a].

When B is azaindole, B can be selected from  ,  , and  , optionally substituted as for heteroaryl[a].

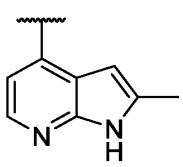
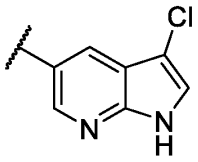
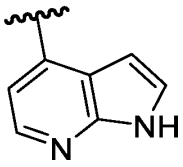
When B is 7-azaindole, B can be selected from  and  , optionally substituted as for heteroaryl[a].

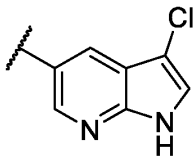
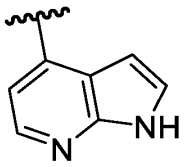
When B is 7-azaindole, B can be  optionally substituted as for heteroaryl[a].

When B is azaindole, B can be selected from  ,  and  , substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

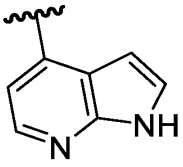
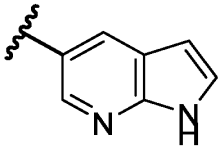
When B is azaindole (particularly 7-azaindole), B can be substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a]. When B is azaindole (particularly 7-azaindole), B can be substituted with alkyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a]. For example, when B is azaindole (particularly 7-azaindole), B can be substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a]. When B is azaindole (particularly 7-azaindole), B can be substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a]. When B is azaindole (particularly 7-azaindole), B can be substituted with

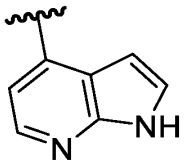
NH_2 and halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

For example, B can be selected from:  ,  and  .

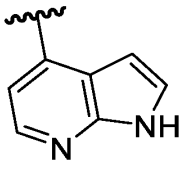
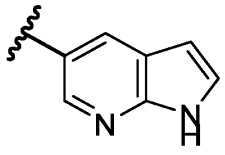
When B is azaindole (particularly 7-azaindole), B can be substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a]. When B is azaindole (particularly 7-azaindole), B can be substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a]. When B is azaindole (particularly 7-azaindole), B can be substituted with NH_2 and halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a]. For example, B can be selected from:  and  .

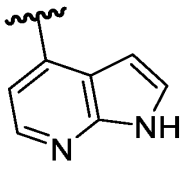
When B is 7-azaindole, B can be substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

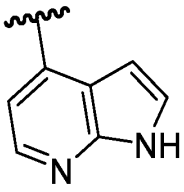
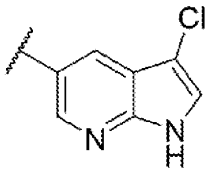
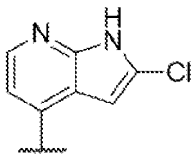
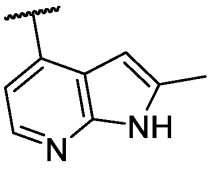
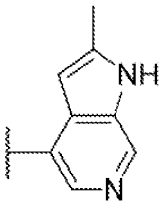
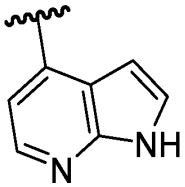
When B is 7-azaindole, B can be selected from  and  , substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

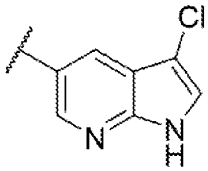
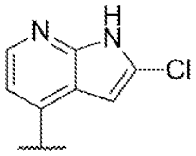
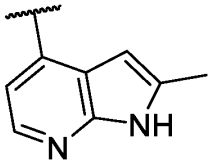
When B is 7-azaindole, B can be  substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

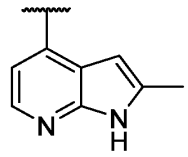
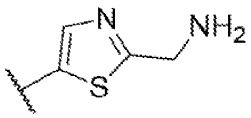
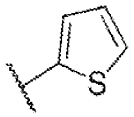
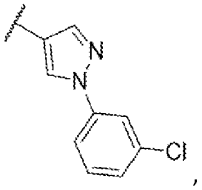
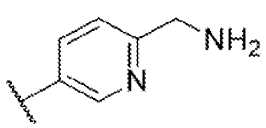
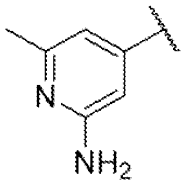
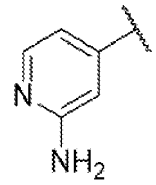
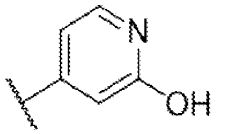
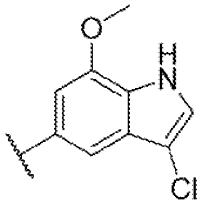
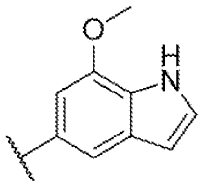
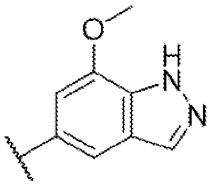
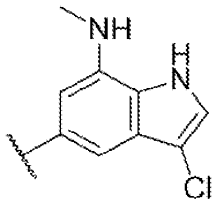
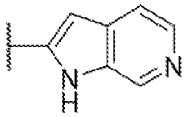
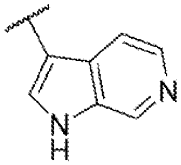
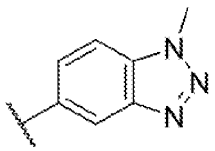
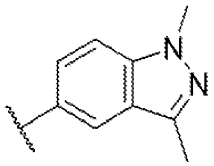
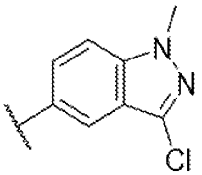
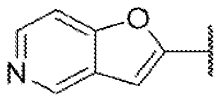
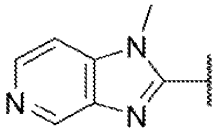
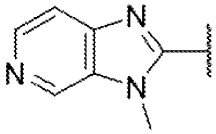
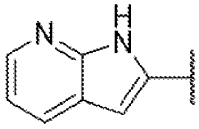
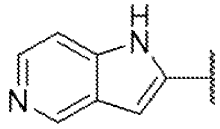
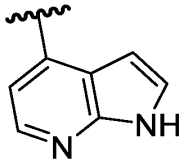
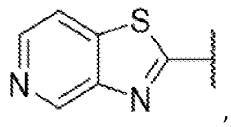
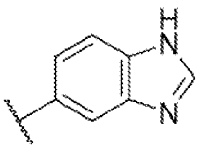
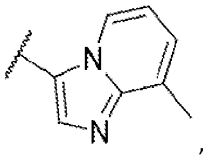
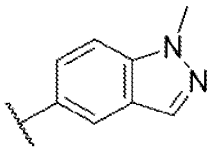
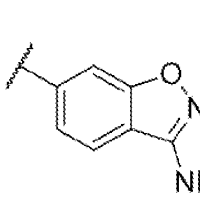
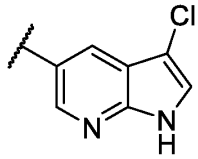
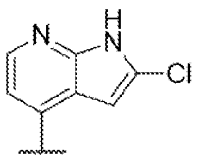
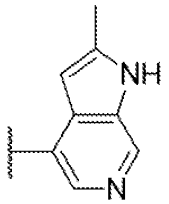
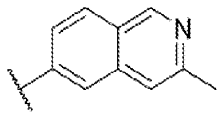
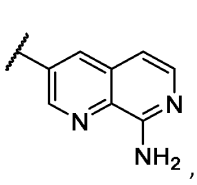
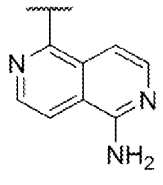
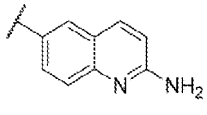
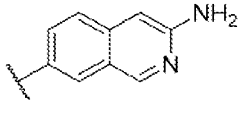
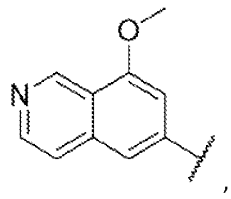
When B is 7-azaindole, B can be substituted with chloro, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

When B is 7-azaindole, B can be selected from  and  , substituted with chloro, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

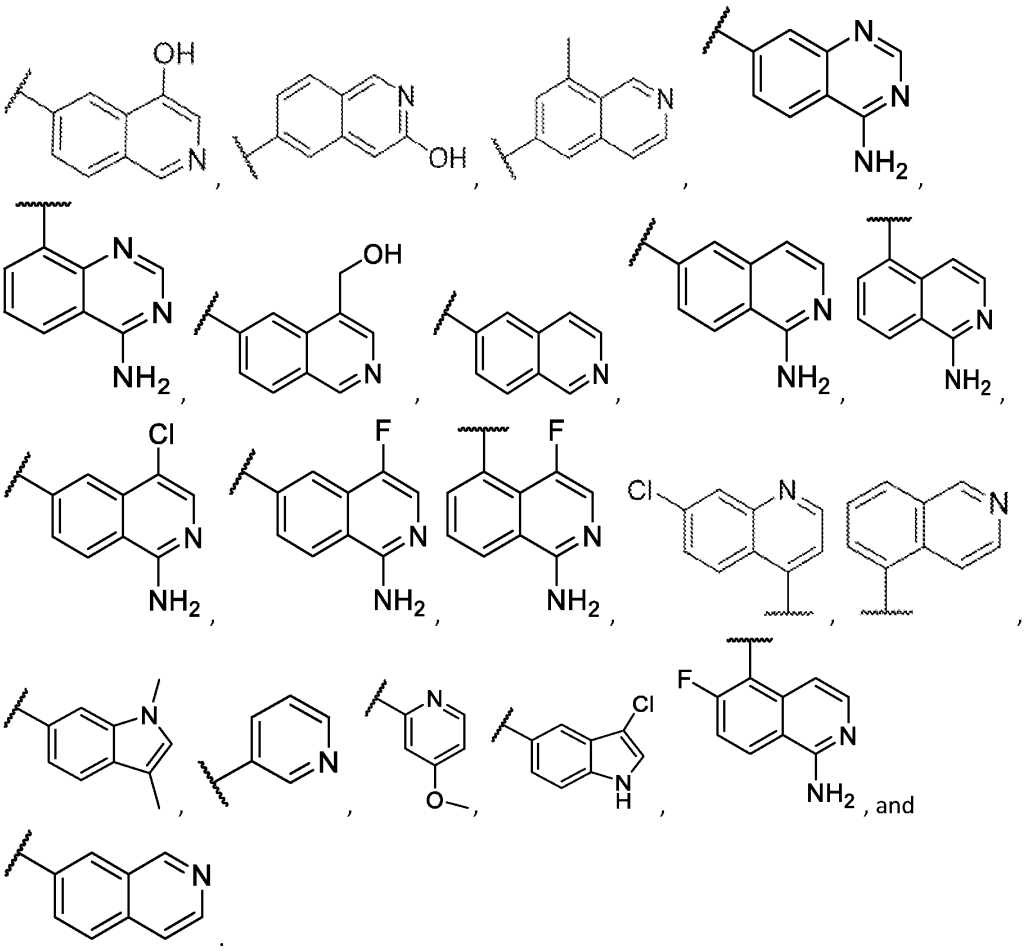
When B is 7-azaindole, B can be  , substituted with chloro, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

When B is azaindole, B can be selected from  ,  ,  ,  ,  , and  .

Preferably when B is 7-azaindole, B can be selected from ,  ,  , and  .

When B is heteroaryl[a], B can selected from  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , 

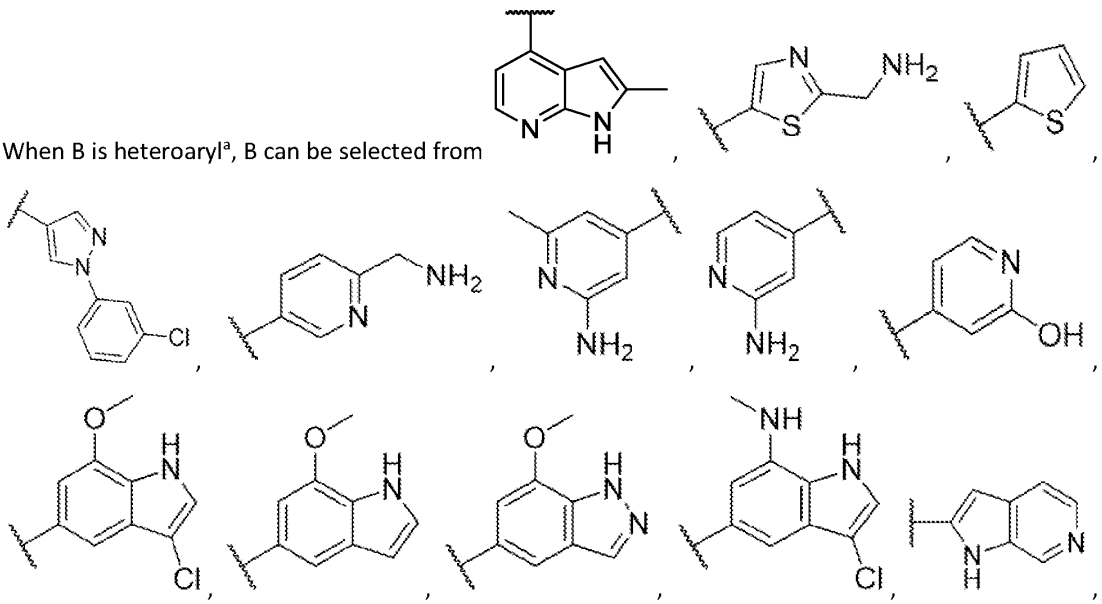
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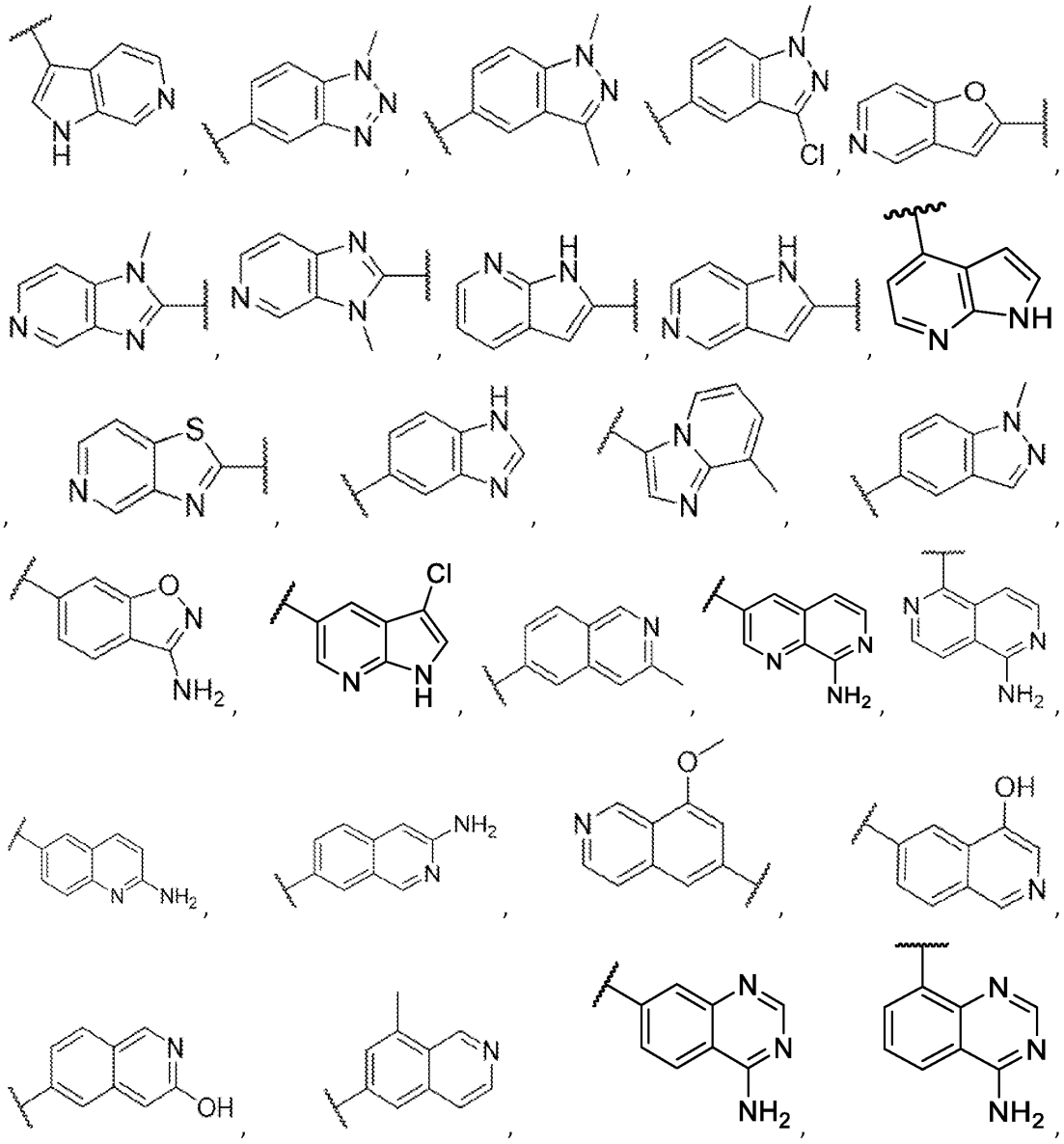


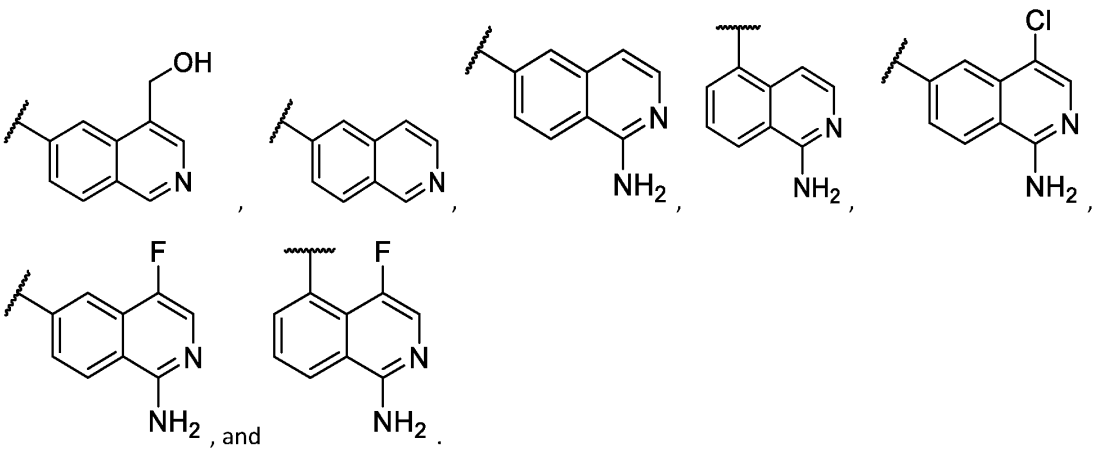
, and

.

When B is heteroaryl[a], B can be selected from

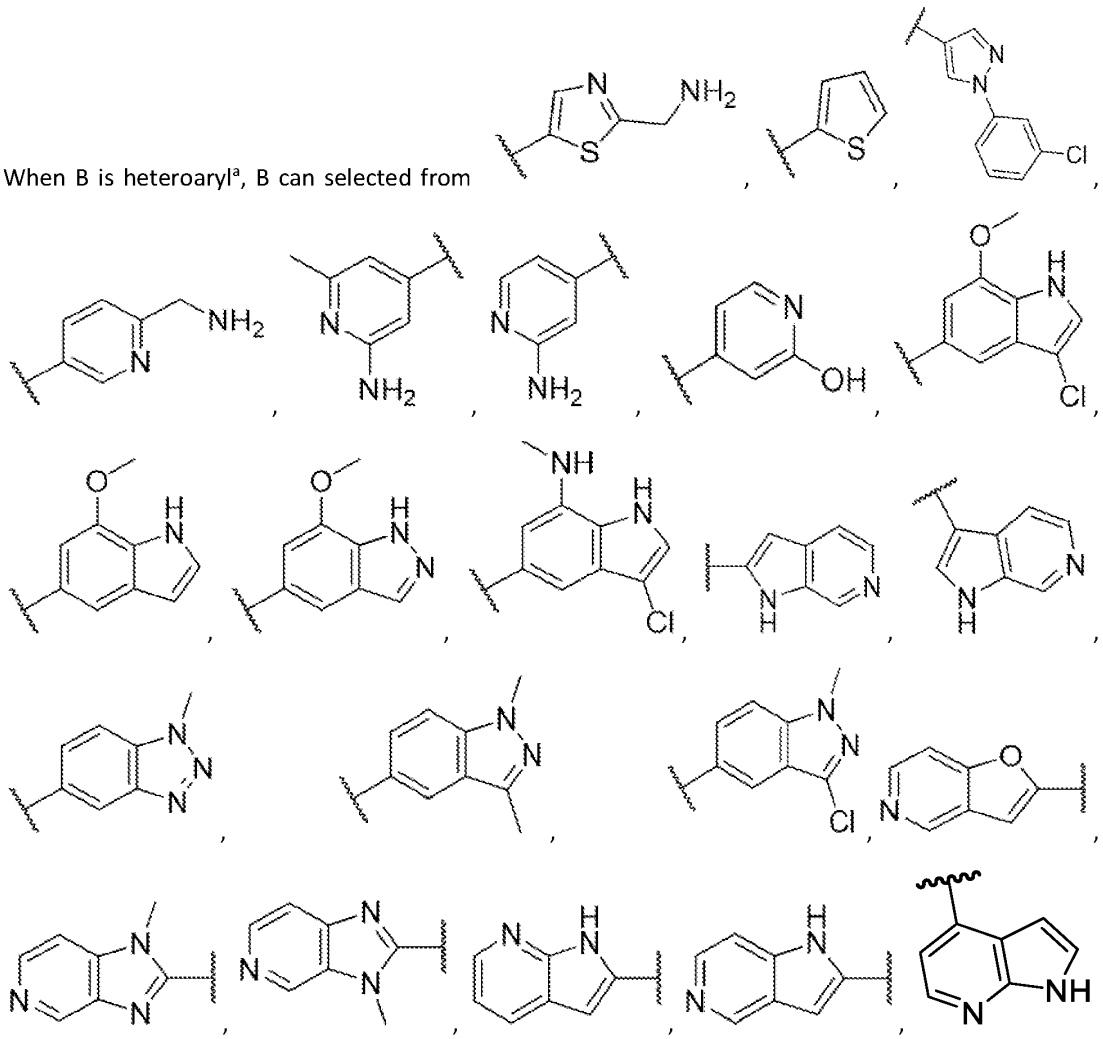


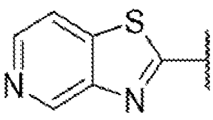
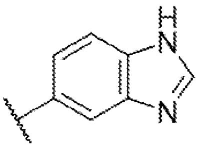
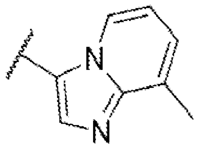
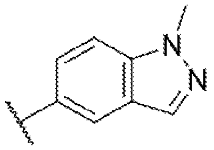


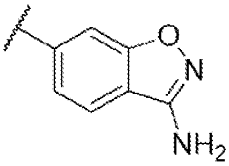
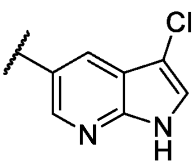
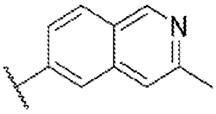
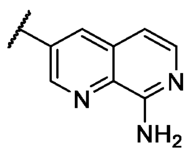
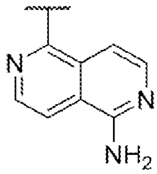


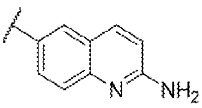
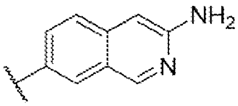
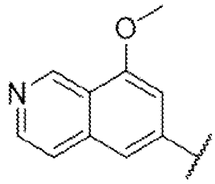
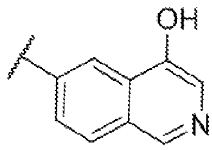
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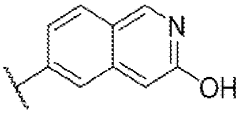
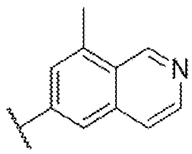
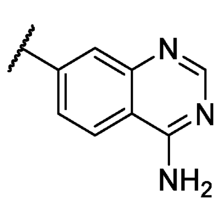
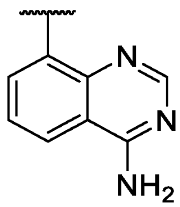
When B is heteroaryl[a], B can selected from

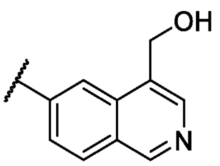
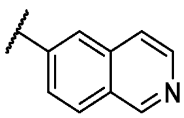
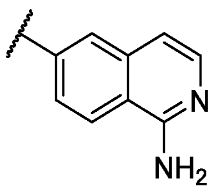
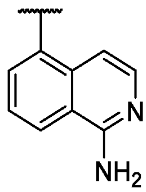
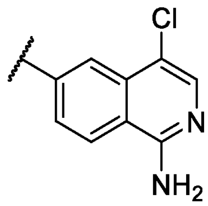


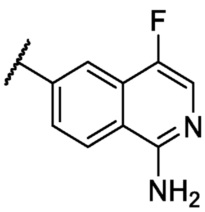
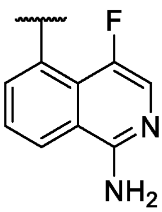
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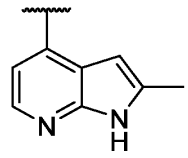
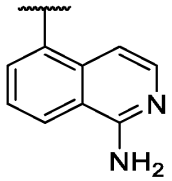
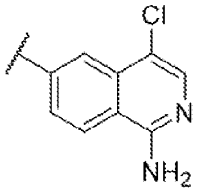
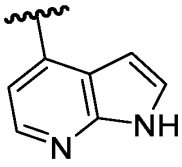
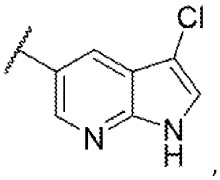
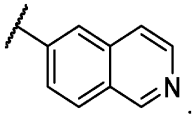
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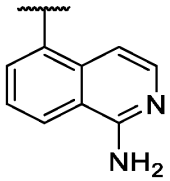
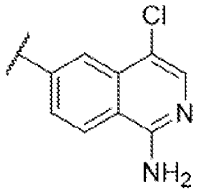
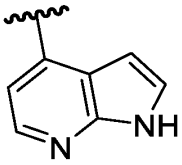
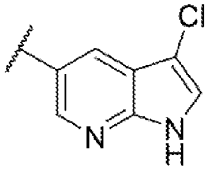
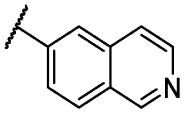
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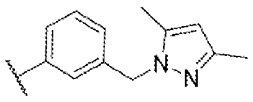
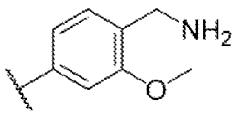
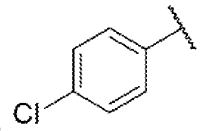
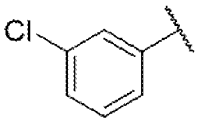
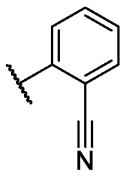
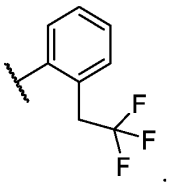
 , and  .

B can be selected from  ,  ,  ,  ,  , and  .

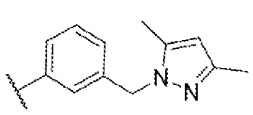
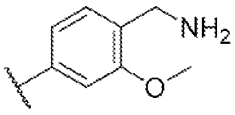
B can be selected from  ,  ,  ,  , and  .

B can be aryl. B can be phenyl or naphthyl, wherein B may be optionally substituted as for aryl. When B is aryl, preferably B is phenyl, wherein B may be optionally substituted as for aryl.

B can be selected from:

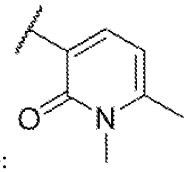
 ,  ,  ,  ,  , and  .

B can be selected from:

 and  .

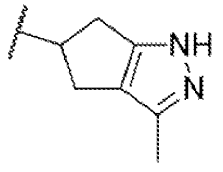
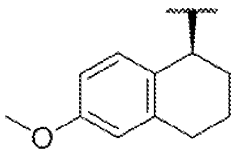
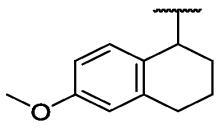
B can be a 5- to 6- membered non-aromatic heterocyclic ring containing one N ring member, which is unsaturated with 1 or 2 double bonds, wherein the non-aromatic heterocyclic ring is optionally substituted by 1, 2 or 3 substituents independently selected from alkyl, alkoxy, aryl^b, OH, OCF_3, halo, oxo, CN, and CF_3.

When B is a 5- to 6- membered non-aromatic heterocyclic ring containing one N ring member, which is unsaturated with 1 or 2 double bonds, it is preferably pyridone (e.g. 2-pyridone or 4-pyridone). B can be pyridone which is unsaturated with 2 double bonds, which may be optionally substituted by 1, 2 or 3 substituents independently selected from alkyl, alkoxy, aryl^b, OH, OCF_3, halo, oxo, CN, and CF_3. B can be pyridone which is unsaturated with 2 double bonds, substituted by two alkyl groups.

B can be:  .

B can be a fused 5,5-, 6,5- or 6,6- bicyclic ring containing an aromatic ring fused to a non-aromatic ring, wherein the bicyclic ring optionally contains one or two N ring members, wherein the fused 5,5-, 6,5- or 6,6- bicyclic ring may be optionally substituted with 1, 2, or 3 substituted by up to three substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, oxo, CN, and CF_3, wherein the 6,5- bicyclic ring may be attached via the 6- or 5- membered ring.

B can be selected from:

 ,  , and  .

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is N or NH; and B is heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is N or NH; and B is isoquinolinyl, optionally substituted as for heteroaryl[a].

Yet more preferably, when not absent, -V-Z- is selected from-CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is N or NH; and B is isoquinolinyl, substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More specifically, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is N or NH; and B is isoquinolinyl, substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is N or NH; and B is heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is N or NH; and B is isoquinolinyl, optionally substituted as for heteroaryl[a].

Yet more preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is N or NH; and B is isoquinolinyl, substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More specifically, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is N or NH; and B is isoquinolinyl, substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is N or NH; and B is heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is N or NH; and B is isoquinolinyl, optionally substituted as for heteroaryl[a].

Yet more preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is N or NH; and B is isoquinolinyl, substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More specifically, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2,

-CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is N or NH; and B is isoquinolinyl, substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is isoquinolinyl, optionally substituted as for heteroaryl[a].

Yet more preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is isoquinolinyl, substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More specifically, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is isoquinolinyl, substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

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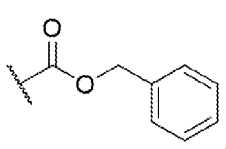
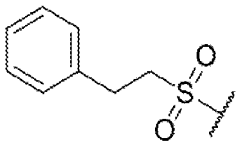
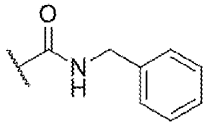
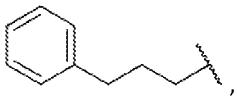
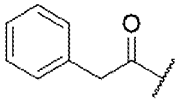
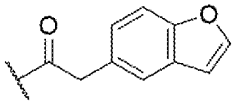
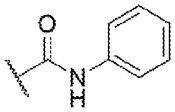
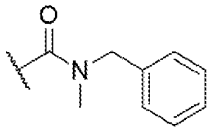
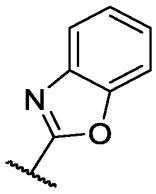
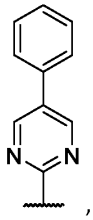
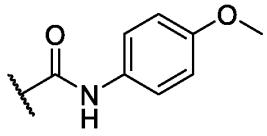
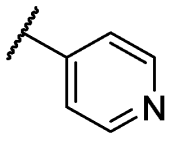
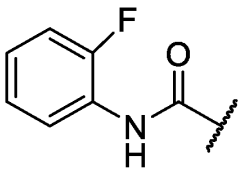
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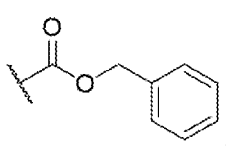
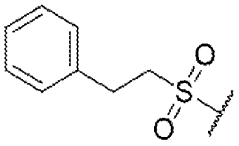
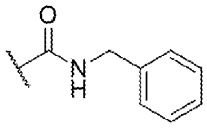
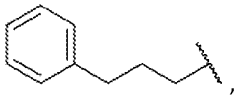
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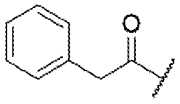
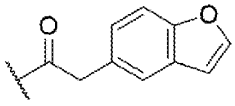
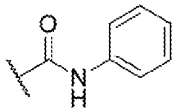
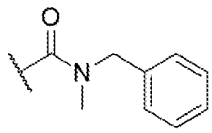
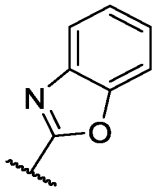

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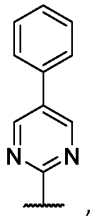
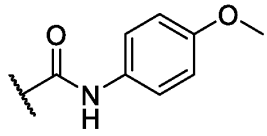
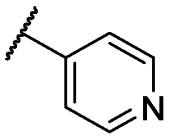
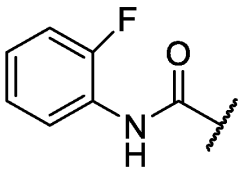
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More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is isoquinolinyl, optionally substituted as for heteroaryl[a].

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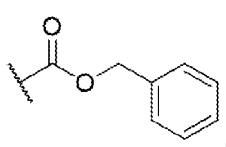
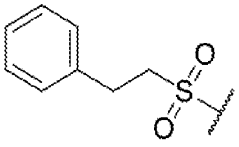
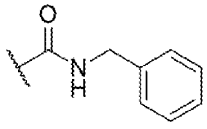
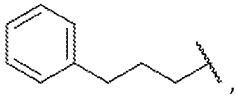
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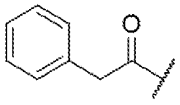
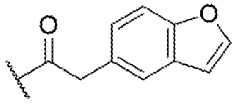
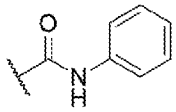
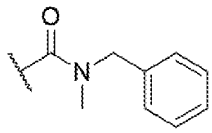
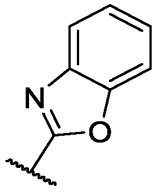
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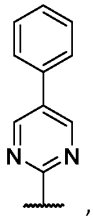
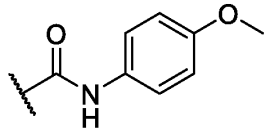
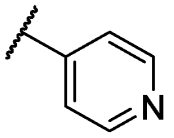
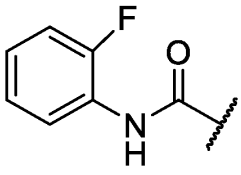
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Preferably, X is CR1R2; R1 is H; R2 is H; Y is NH; and B is heteroaryl[a]. More preferably, X is CR1R2; R1 is H; R2 is H; Y is NH; and B is isoquinolinyl, optionally substituted as for heteroaryl[a]. Yet more preferably, X is CR1R2; R1 is H; R2 is H; Y is NH; and B is isoquinolinyl, substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a]. More specifically, X is CR1R2; R1 is H; R2 is H; Y is NH; and B is isoquinolinyl, substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is quinolinyl, optionally substituted as for heteroaryl[a].

Yet more preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is quinolinyl, substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More specifically, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is quinolinyl, substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is quinolinyl, optionally substituted as for heteroaryl[a].

Yet more preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is quinolinyl, substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

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$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is quinolinyl, substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is heteroaryl[a].

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More specifically, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is quinolinyl, substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is NH; and B is heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is NH; and B is quinolinyl, optionally substituted as for heteroaryl[a].

Yet more preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

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wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is NH; and B is quinolinyl, substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

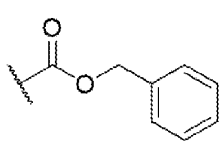
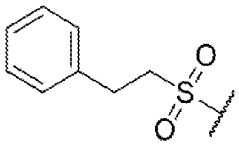
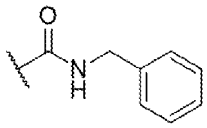
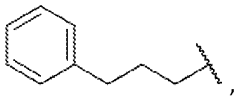
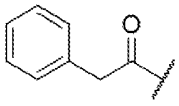
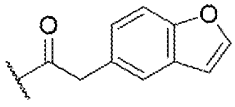
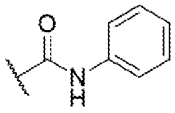
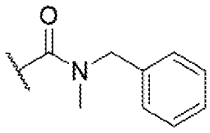
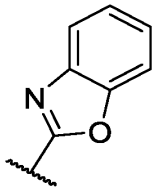
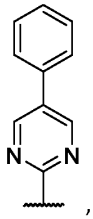
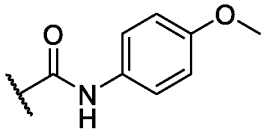
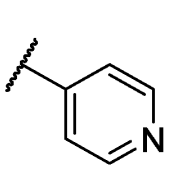
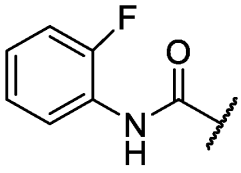
More specifically, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

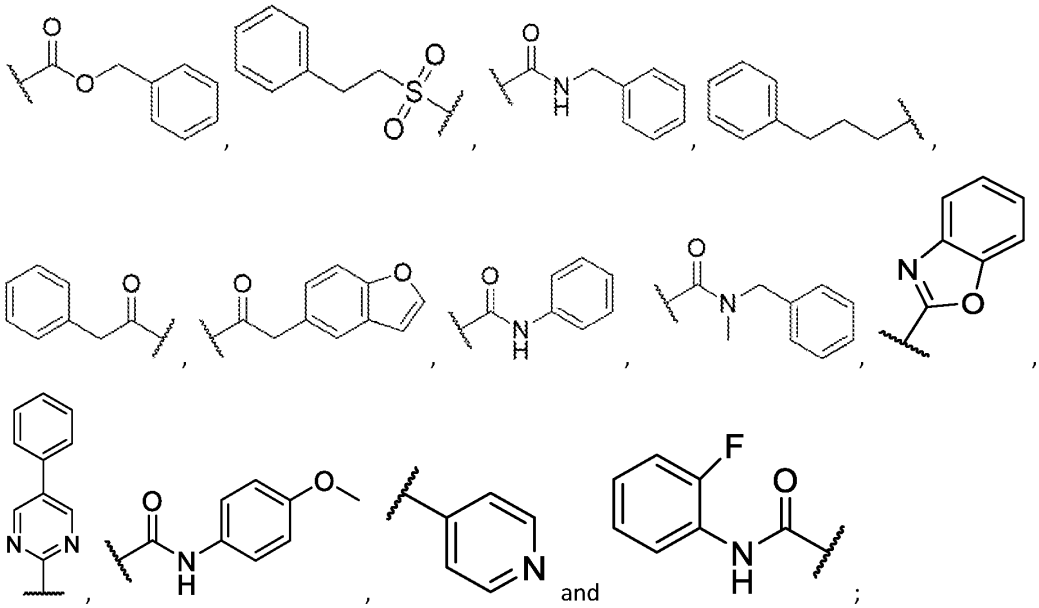
X is CR1R2; R1 is H; R2 is H; Y is NH; and B is quinolinyl, substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:


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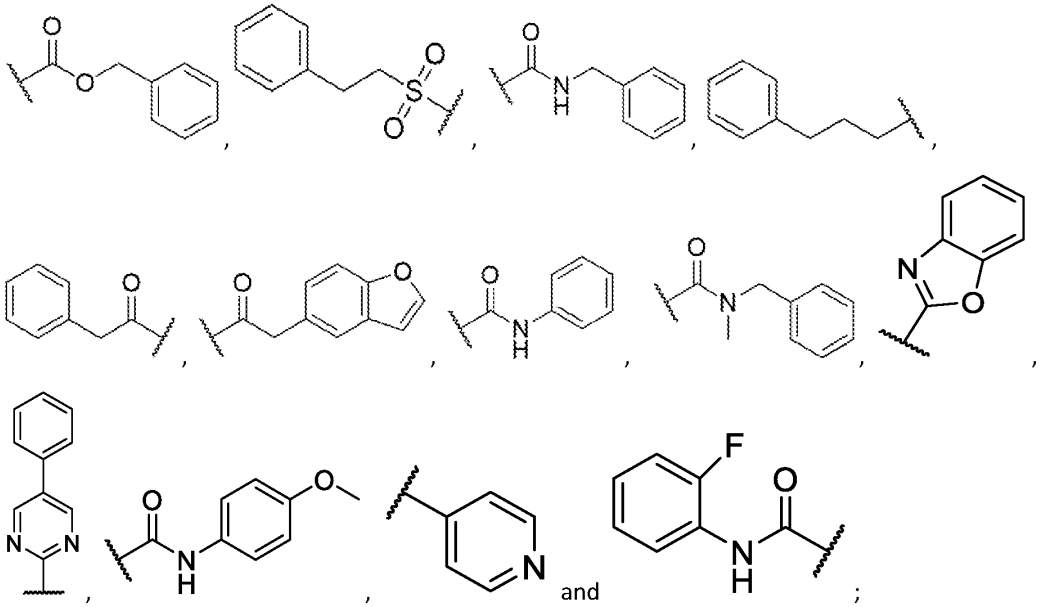
X is CR1R2; R1 is H; R2 is H; Y is NH; and B is heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



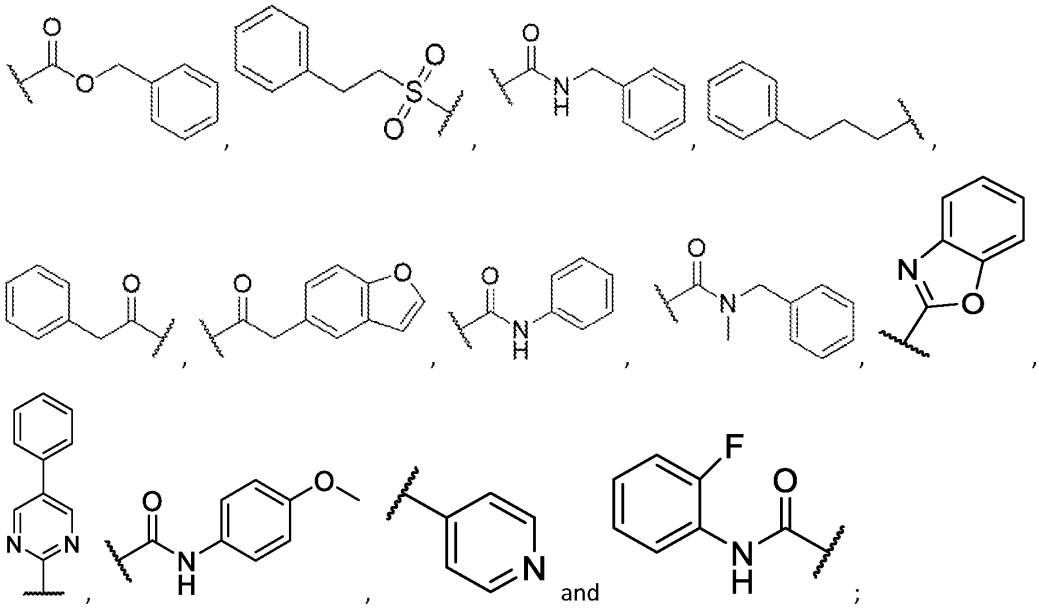
X is CR1R2; R1 is H; R2 is H; Y is NH; and B is quinolinyl, optionally substituted as for heteroaryl[a].

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X is CR1R2; R1 is H; R2 is H; Y is NH; and B is quinolinyl, substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More specifically, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



X is CR1R2; R1 is H; R2 is H; Y is NH; and B is quinolinyl, substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is quinolinyl, optionally substituted as for heteroaryl[a].

Yet more preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is quinolinyl, substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More specifically, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is quinolinyl, substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, X is CR1R2; R1 is H; R2 is H; Y is NH; and B is heteroaryl[a]. More preferably, X is CR1R2; R1 is H; R2 is H; Y is NH; and B is quinolinyl, optionally substituted as for heteroaryl[a]. Yet more preferably, X is CR1R2; R1 is H; R2 is H; Y is NH; and B is quinolinyl, substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a]. More specifically, X is CR1R2; R1 is H; R2 is H; Y is NH; and B is quinolinyl, substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is azaindole (particularly 7-azaindole), optionally substituted as for heteroaryl[a].

Yet more preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is azaindole (particularly 7-azaindole), substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is azaindole (particularly 7-azaindole) substituted with alkyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is azaindole (particularly

7-azaindole), substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[b].

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is azaindole (particularly 7-azaindole) substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More specifically, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is azaindole (particularly 7-azaindole), substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is azaindole (particularly 7-azaindole), optionally substituted as for heteroaryl[a].

Yet more preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is azaindole (particularly 7-azaindole), substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is azaindole (particularly 7-azaindole) substituted with alkyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is azaindole (particularly 7-azaindole), substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[b].

Preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is azaindole (particularly 7-azaindole) substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More specifically, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is azaindole (particularly

7-azaindole), substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), optionally substituted as for heteroaryl[a].

Yet more preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole) substituted with alkyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[b].

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole) substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More specifically, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$,

-CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is NH; and B is heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), optionally substituted as for heteroaryl[a].

Yet more preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole) substituted with alkyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[b].

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole) substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

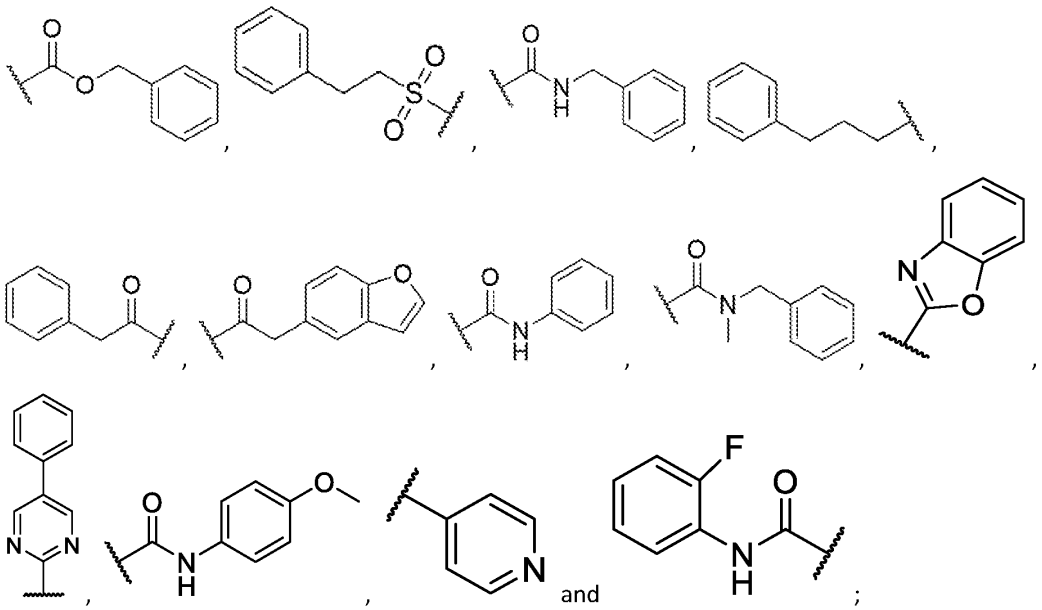
More specifically, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

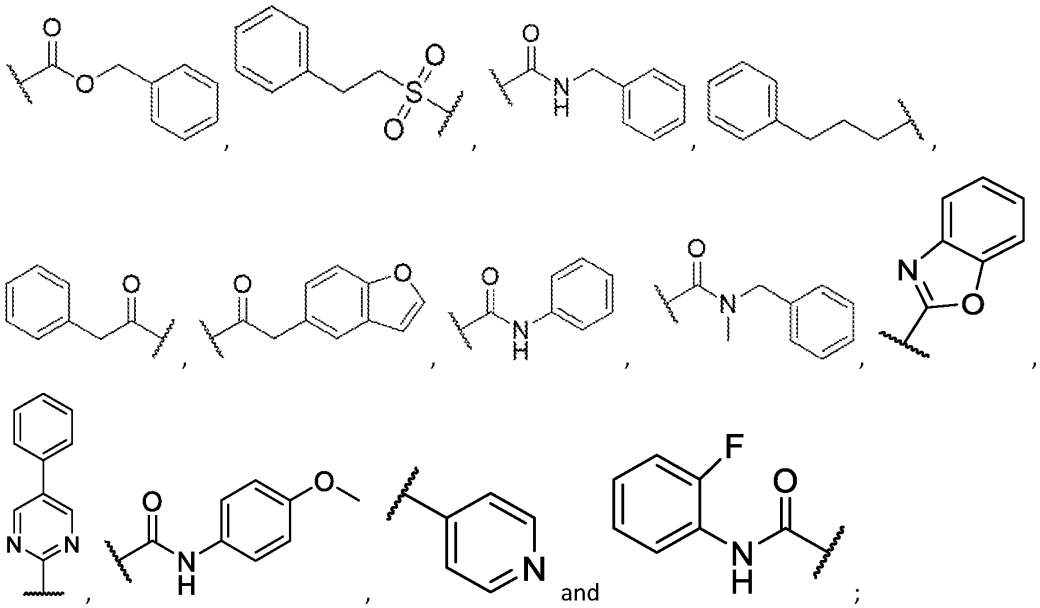
X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



X is CR1R2; R1 is H; R2 is H; Y is NH; and B is heteroaryl[a].

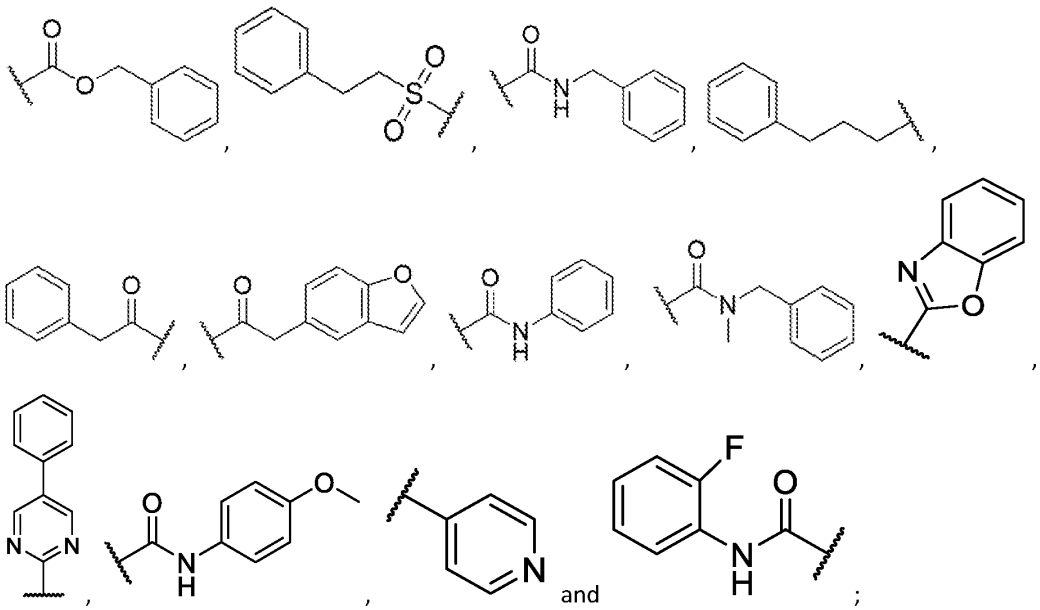
More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



and ;

X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), optionally substituted as for heteroaryl[a].

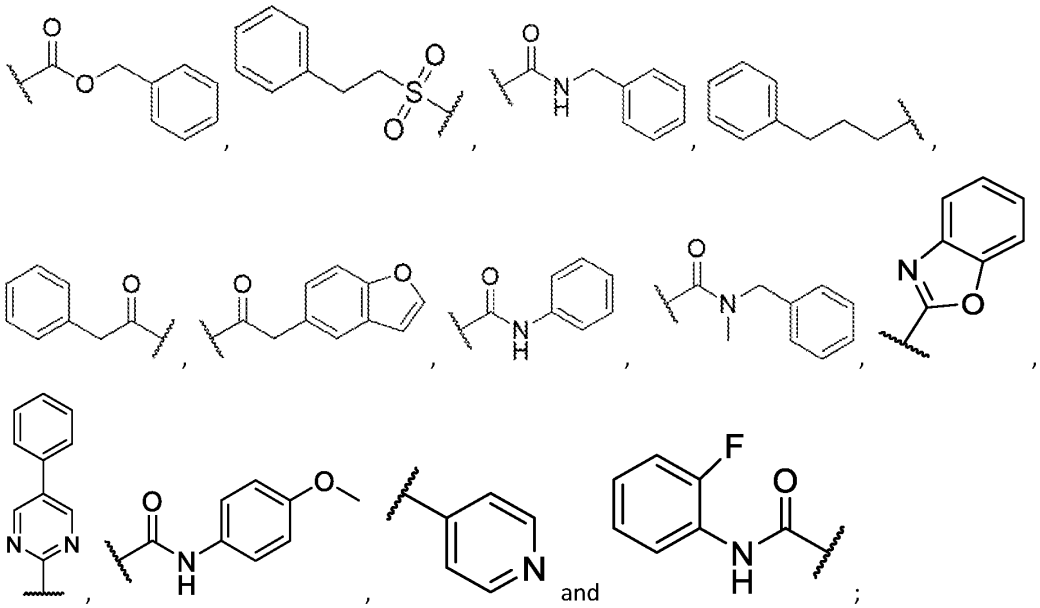
Yet more preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



and ;

X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

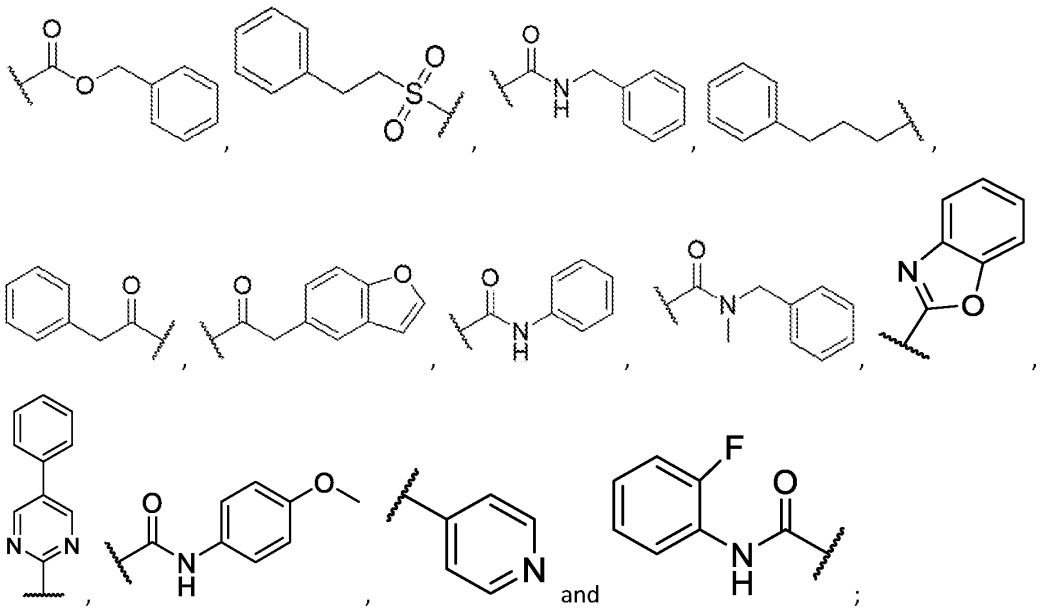
Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



and ;

X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole) substituted with alkyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

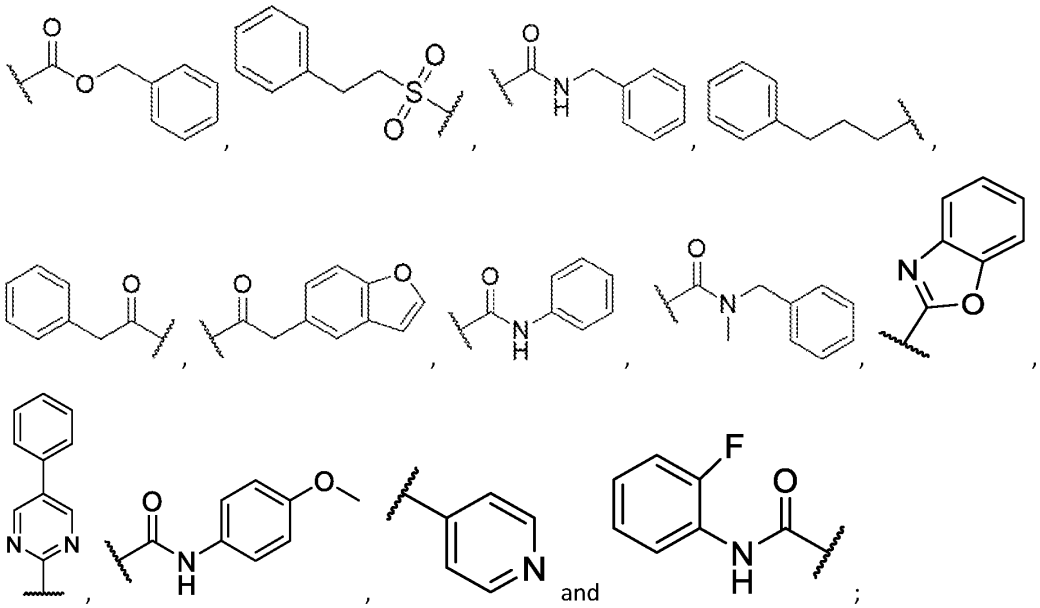
Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



and ;

X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[b].

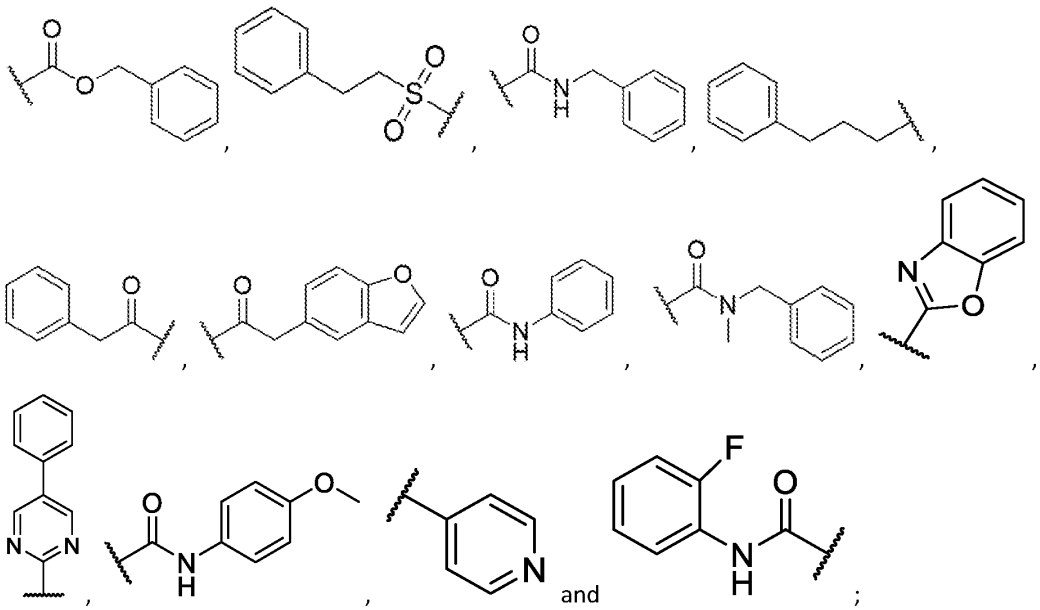
Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



and ;

X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole) substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More specifically, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



and ;

X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), optionally substituted as for heteroaryl[a].

Yet more preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole) substituted with alkyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[b].

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole) substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More specifically, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, X is CR1R2; R1 is H; R2 is H; Y is NH; and B is heteroaryl[a]. More preferably, X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), optionally substituted as for heteroaryl[a]. Yet more preferably, X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a]. Alternatively, X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole) substituted with alkyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a]. Alternatively, X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[b]. Preferably, X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole) substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a]. More specifically, X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-,

-$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is azaindole (particularly 7-azaindole), optionally substituted as for heteroaryl[a].

Yet more preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is azaindole (particularly 7-azaindole), substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is azaindole (particularly 7-azaindole), substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[b].

More specifically, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is azaindole (particularly 7-azaindole), substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is azaindole (particularly 7-azaindole), optionally substituted as for heteroaryl[a].

Yet more preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is azaindole (particularly 7-azaindole), substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is azaindole (particularly 7-azaindole), substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[b].

More specifically, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

X is CR1R2; R1 is H; R2 is H; Y is NH or N; and B is azaindole (particularly 7-azaindole), substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), optionally substituted as for heteroaryl[a].

Yet more preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[b].

More specifically, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is NH; and B is heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), optionally substituted as for heteroaryl[a].

Yet more preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[b].

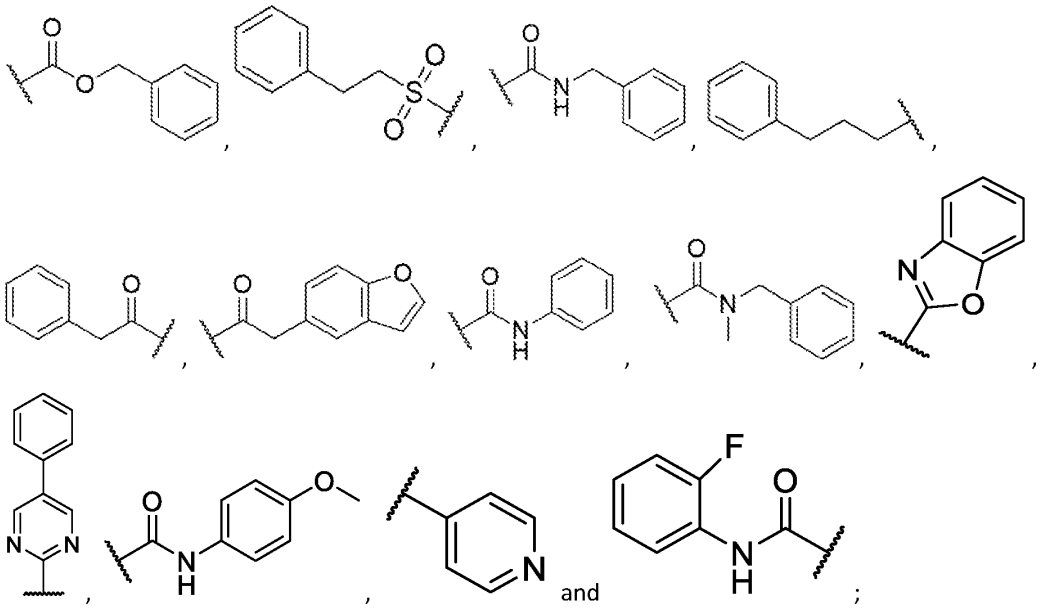
More specifically, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

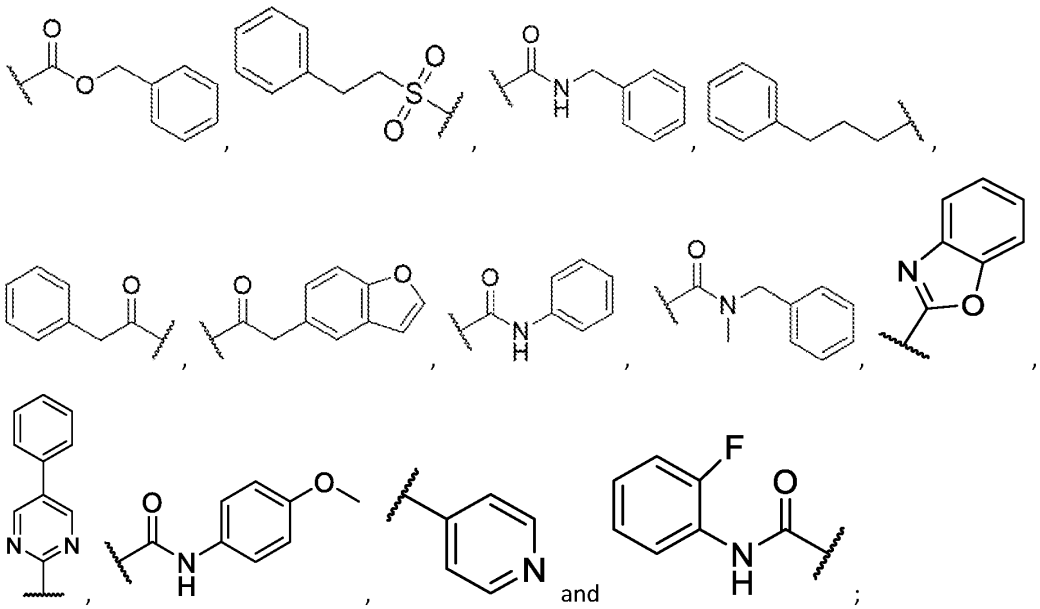
Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



and ;

X is CR1R2; R1 is H; R2 is H; Y is NH; and B is heteroaryl[a].

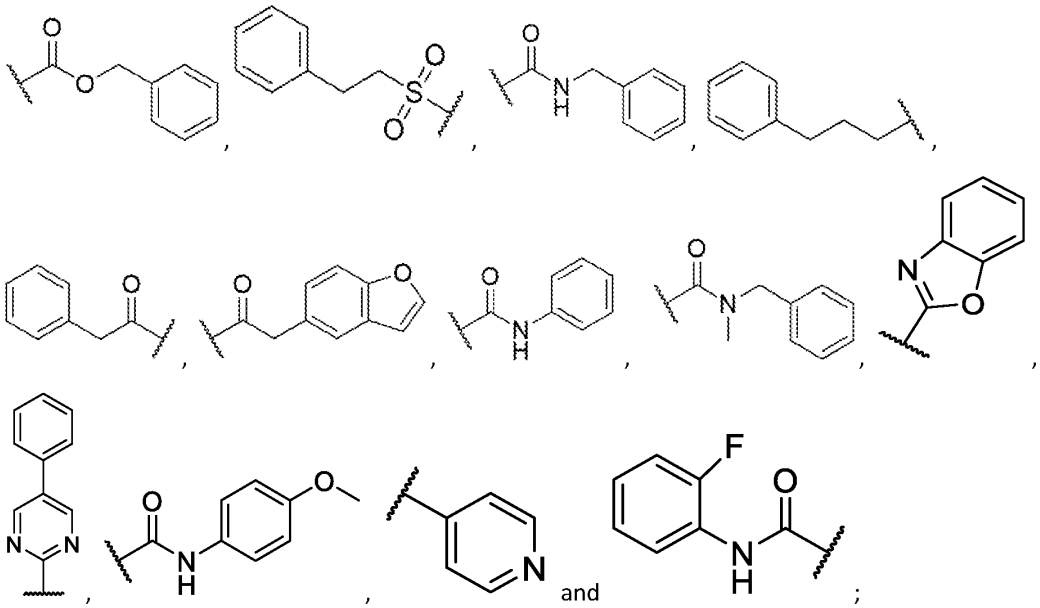
More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



and ;

X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), optionally substituted as for heteroaryl[a].

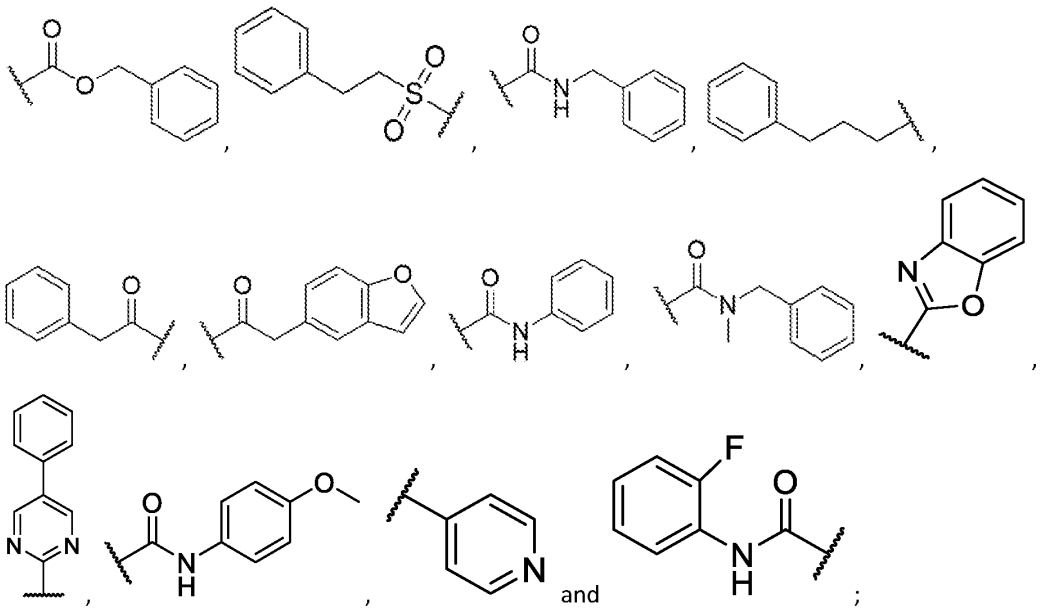
Yet more preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



and ;

X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

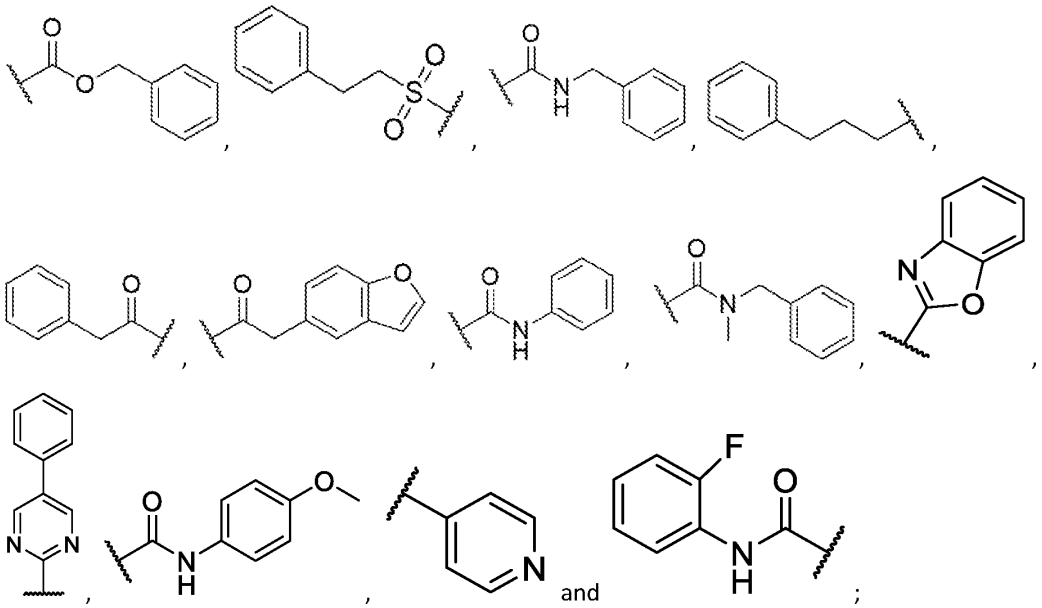
Alternatively, -V-Z- is selected from --CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



and ;

X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[b].

More specifically, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), optionally substituted as for heteroaryl[a].

Yet more preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[b].

More specifically, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, X is CR1R2; R1 is H; R2 is H; Y is NH; and B is heteroaryl[a]. More preferably, X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), optionally substituted as for heteroaryl[a]. Yet

more preferably, X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a]. Alternatively, X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[b]. More specifically, X is CR1R2; R1 is H; R2 is H; Y is NH; and B is azaindole (particularly 7-azaindole), substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];
X is CR1R2; R1 is H; R2 is H; Y is O; and B is heteroaryl[a].
More preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];
X is CR1R2; R1 is H; R2 is H; Y is O; and B is isoquinolinyl, optionally substituted as for heteroaryl[a].
Yet more preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];
X is CR1R2; R1 is H; R2 is H; Y is O; and B is isoquinolinyl, substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].
More specifically, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];
X is CR1R2; R1 is H; R2 is H; Y is O; and B is isoquinolinyl, substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$,

-$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is isoquinolinyl, optionally substituted as for heteroaryl[a].

Yet more preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is isoquinolinyl, substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More specifically, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is isoquinolinyl, substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is isoquinolinyl, optionally substituted as for heteroaryl[a].

Yet more preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-,

-$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is isoquinolinyl, substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More specifically, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is isoquinolinyl, substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

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$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is isoquinolinyl, optionally substituted as for heteroaryl[a].

Yet more preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is isoquinolinyl, substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More specifically, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is isoquinolinyl, substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is isoquinolinyl, optionally substituted as for heteroaryl[a].

Yet more preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is isoquinolinyl, substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More specifically, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is isoquinolinyl, substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, X is CR1R2; R1 is H; R2 is H; Y is O; and B is heteroaryl[a]. More preferably, X is CR1R2; R1 is H; R2 is H; Y is O; and B is isoquinolinyl, optionally substituted as for heteroaryl[a]. Yet more preferably, X is CR1R2; R1 is H; R2 is H; Y is O; and B is isoquinolinyl, substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a]. More specifically, X is CR1R2; R1 is H; R2 is H; Y is O; and B is isoquinolinyl, substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is quinolinyl, optionally substituted as for heteroaryl[a].

Yet more preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2,

$-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is quinolinyl, substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More specifically, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is quinolinyl, substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is quinolinyl, optionally substituted as for heteroaryl[a].

Yet more preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is quinolinyl, substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More specifically, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is quinolinyl, substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is O; and B is heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is O; and B is quinolinyl, optionally substituted as for heteroaryl[a].

Yet more preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is O; and B is quinolinyl, substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More specifically, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is O; and B is quinolinyl, substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, -V-Z- is selected from $-CH_2-$, $-O-CH_2-$, $-CH_2-O-$, $-CH_2-CH_2-O-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is heteroaryl[a].

More preferably, -V-Z- is selected from $-CH_2-$, $-O-CH_2-$, $-CH_2-O-$, $-CH_2-CH_2-O-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is quinolinyl, optionally substituted as for heteroaryl[a].

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$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is quinolinyl, substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

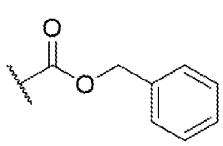
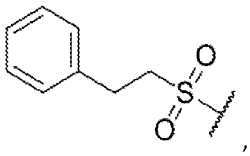
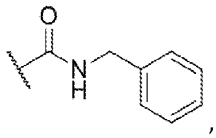
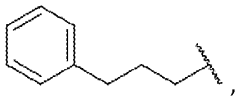
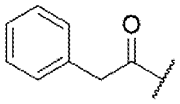
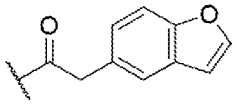
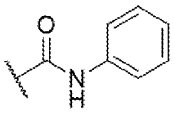
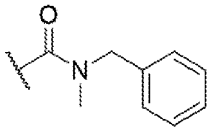
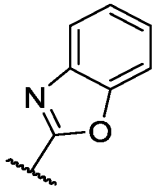
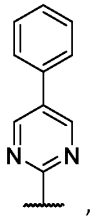
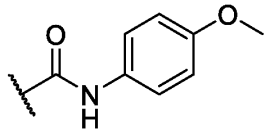
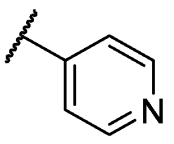
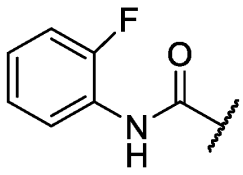
More specifically, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

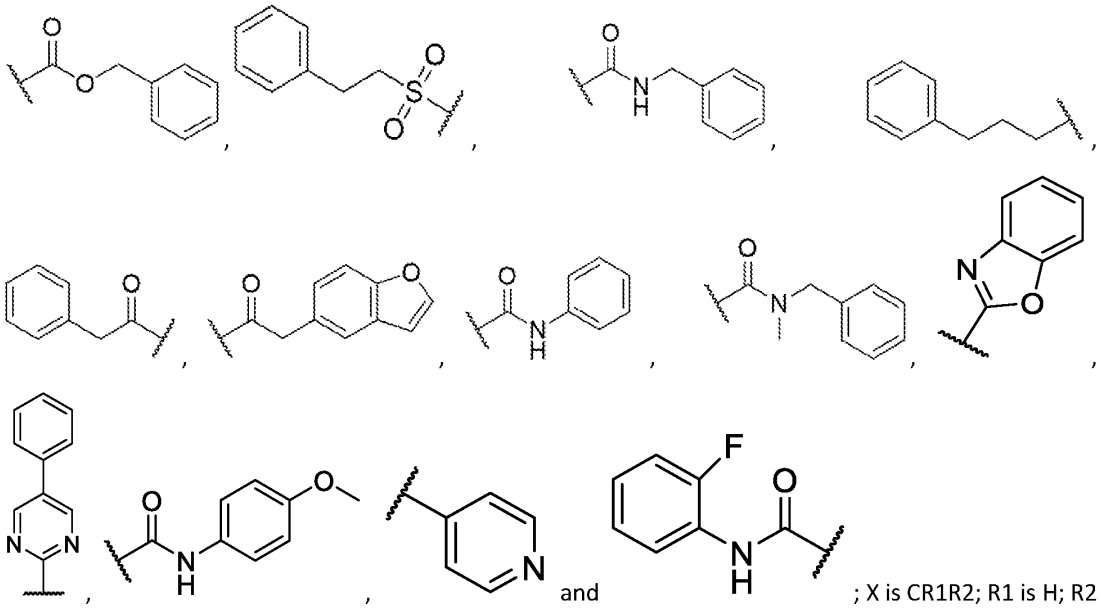
wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is quinolinyl, substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

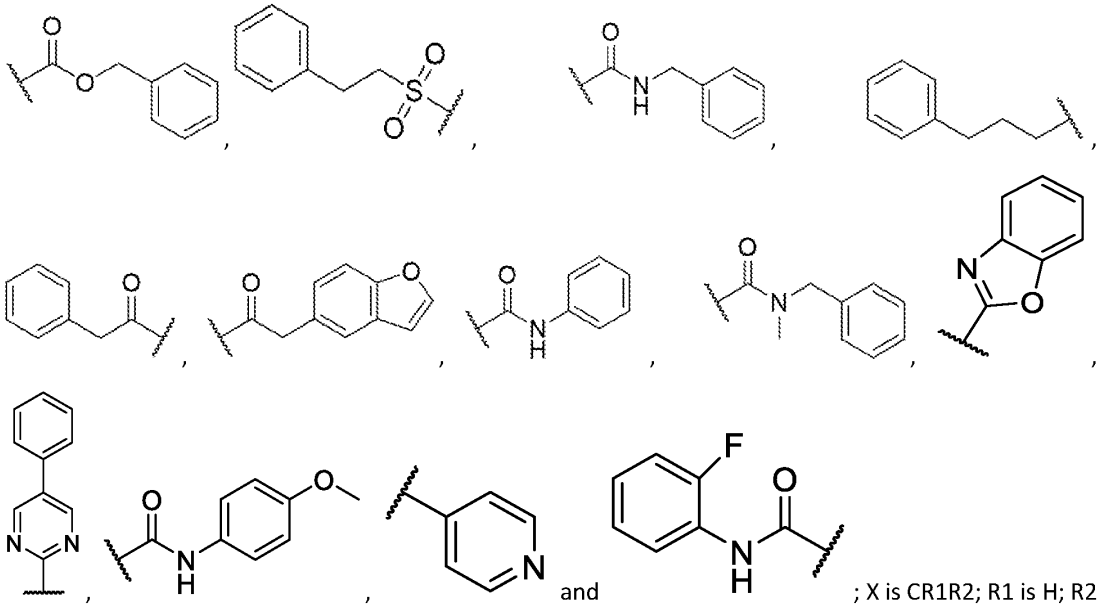













and ; X is CR1R2; R1 is H; R2 is H; Y is O; and B is heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



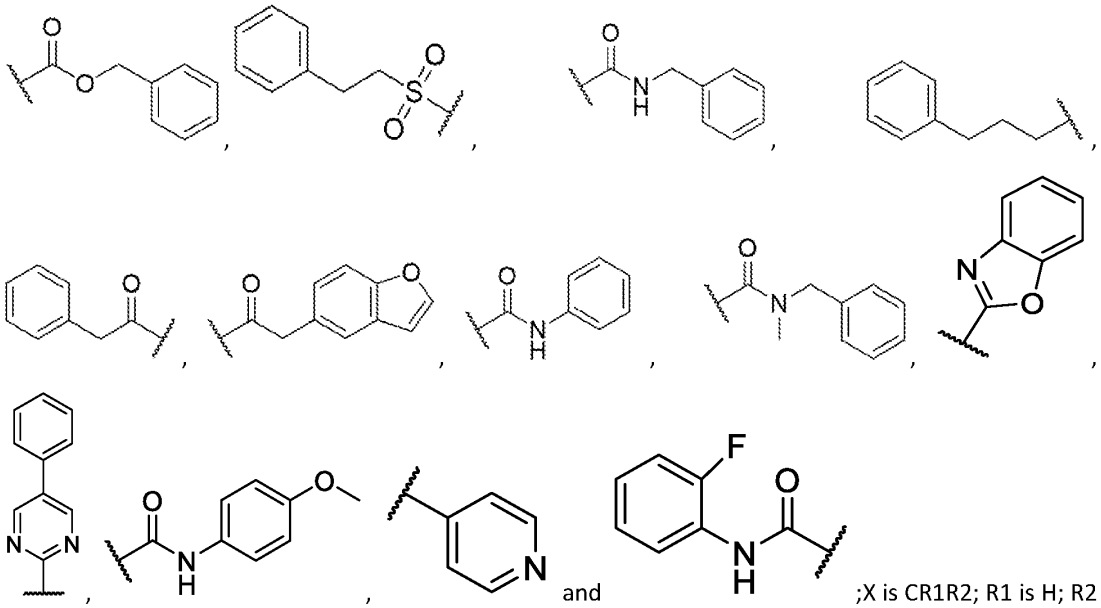
; X is CR1R2; R1 is H; R2 is H; Y is O; and B is quinolinyl, optionally substituted as for heteroaryl[a].

Yet more preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



; X is CR1R2; R1 is H; R2 is H; Y is O; and B is quinolinyl, substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More specifically, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



;X is CR1R2; R1 is H; R2 is H; Y is O; and B is quinolinyl, substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is quinolinyl, optionally substituted as for heteroaryl[a].

Yet more preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is quinolinyl, substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More specifically, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is quinolinyl, substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, X is CR1R2; R1 is H; R2 is H; Y is O; and B is heteroaryl[a]. More preferably, X is CR1R2; R1 is H; R2 is H; Y is O; and B is quinolinyl, optionally substituted as for heteroaryl[a]. Yet more preferably, X is CR1R2; R1 is H; R2 is H; Y is O; and B is quinolinyl, substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a]. More specifically, X is CR1R2; R1 is H; R2 is H; Y is O; and B is quinolinyl, substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), optionally substituted as for heteroaryl[a].

Yet more preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with alkyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[b].

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$,

-$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More specifically, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), optionally substituted as for heteroaryl[a].

Yet more preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-,

-$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with alkyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[b].

Preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More specifically, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2,

-CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), optionally substituted as for heteroaryl[a].

Yet more preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with alkyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[b].

Preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More specifically, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, -V-Z- is selected from CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is heteroaryl[a].

More preferably, -V-Z- is selected from CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), optionally substituted as for heteroaryl[a].

Yet more preferably, -V-Z- is selected from CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, -V-Z- is selected from CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

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Preferably, -V-Z- is selected from CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

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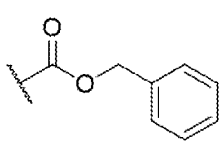
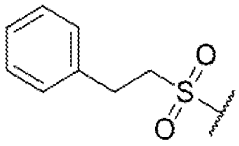
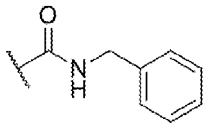
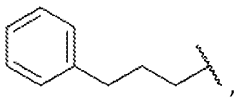
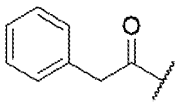
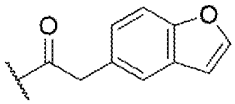
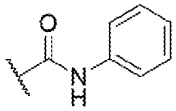
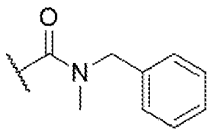
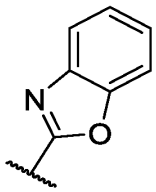
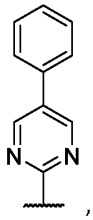
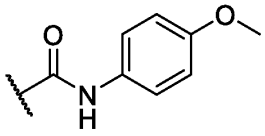
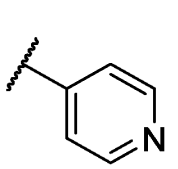
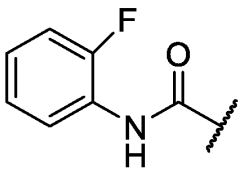
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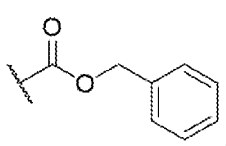
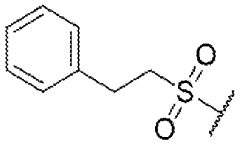
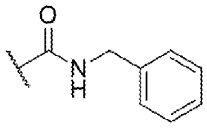
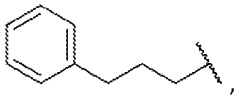
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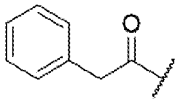
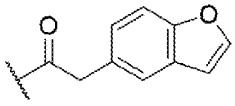
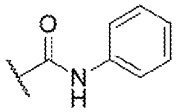
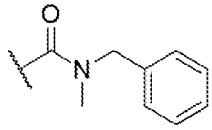
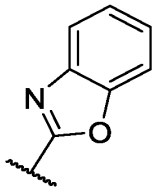
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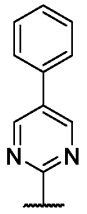
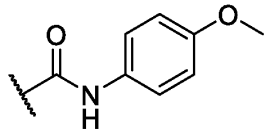
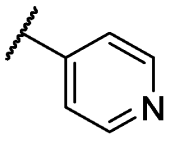
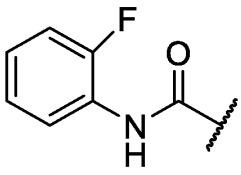

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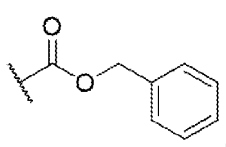
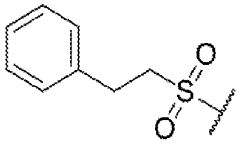
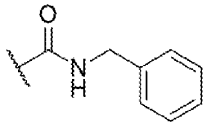
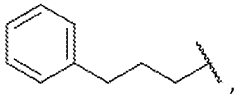
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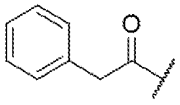
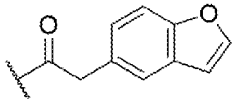
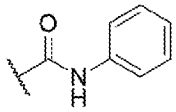
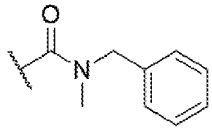
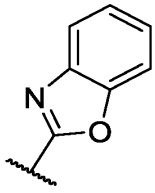
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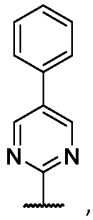
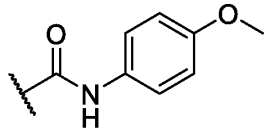
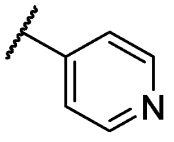
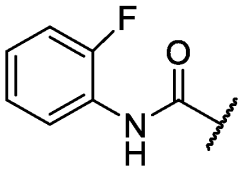
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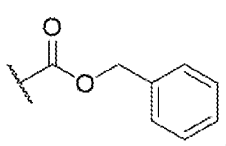
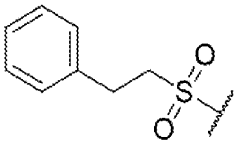
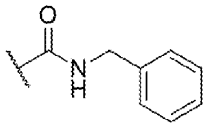
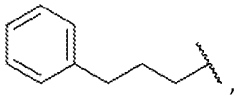
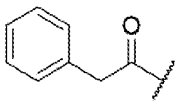
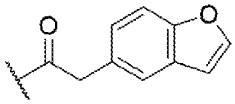
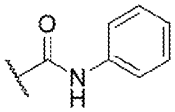
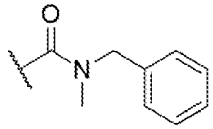
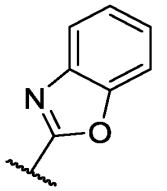
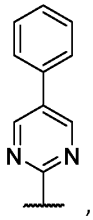
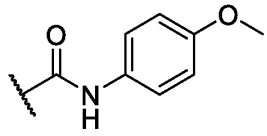
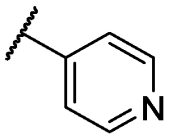
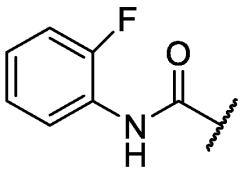
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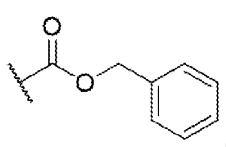
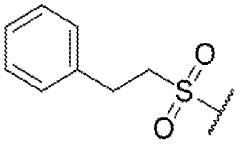
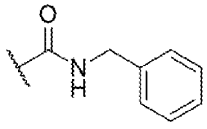
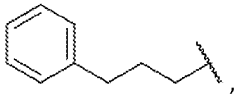
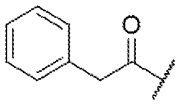
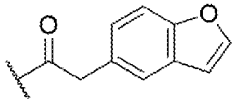
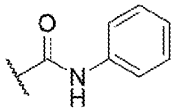
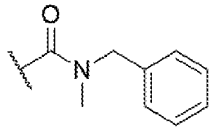
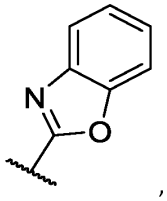
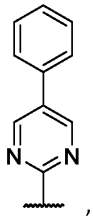
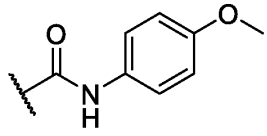
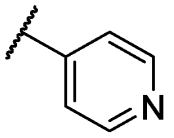
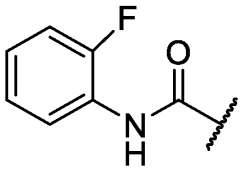
X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

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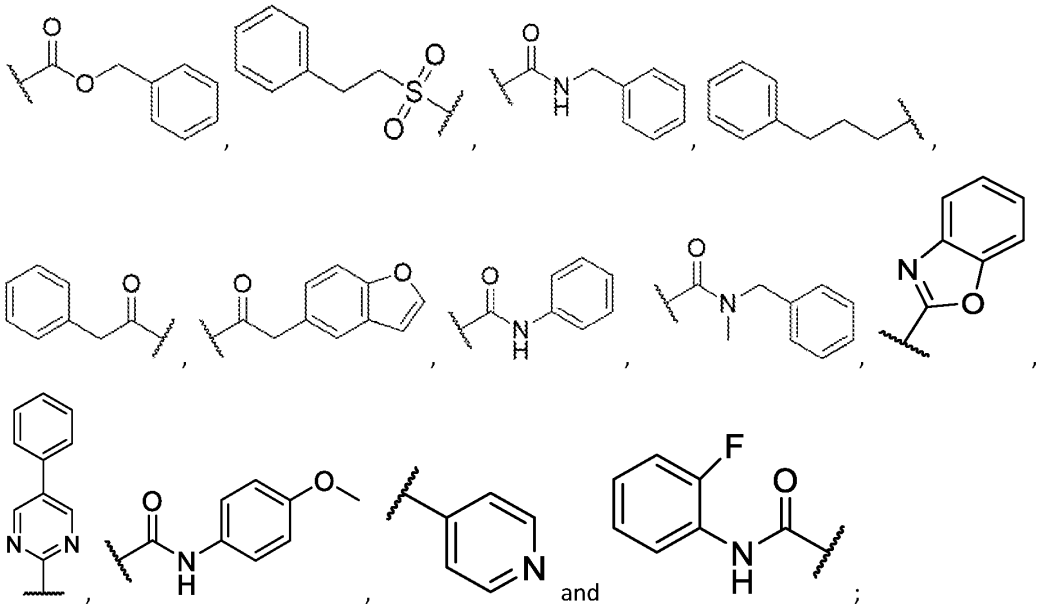
X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with alkyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

 ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  and  ;

X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[b].

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), optionally substituted as for heteroaryl[a].

Yet more preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with alkyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[b].

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More specifically, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, X is CR1R2; R1 is H; R2 is H; Y is O; and B is heteroaryl[a]. More preferably, X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), optionally substituted as for heteroaryl[a]. Yet more preferably, X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a]. Alternatively, X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with alkyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a]. Alternatively, X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[b]. Preferably, X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a]. More specifically, X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];
X is CR1R2; R1 is H; R2 is H; Y is O; and B is heteroaryl[a].
More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];
X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), optionally substituted as for heteroaryl[a].
Yet more preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: --CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[b].

More specifically, when not absent, -V-Z- is selected from: --CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), optionally substituted as for heteroaryl[a].

Yet more preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: --CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2,

$-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[b].

More specifically, when not absent, -V-Z- is selected from: $--CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

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Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is O; and B is heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), optionally substituted as for heteroaryl[a].

Yet more preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$; X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[b].

More specifically, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$,

-CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), optionally substituted as for heteroaryl[a].

Yet more preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[b].

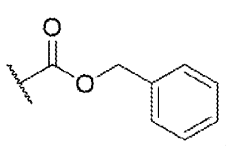
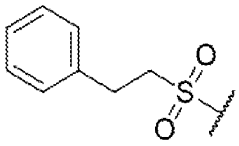
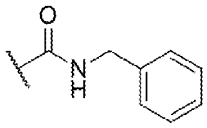
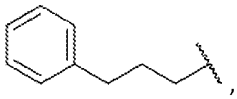
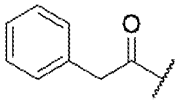
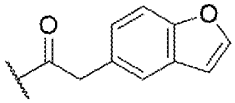
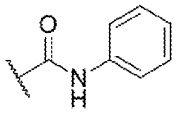
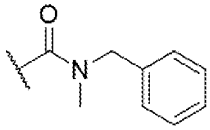
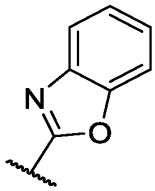
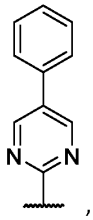
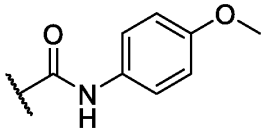
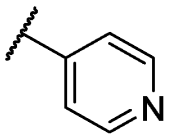
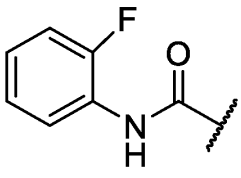
More specifically, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

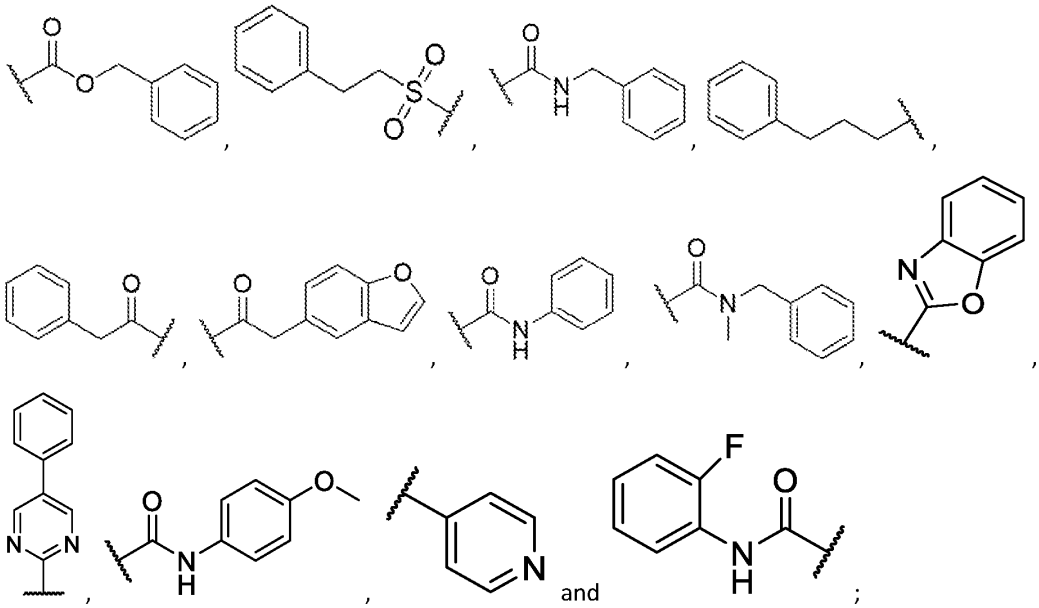
X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, -V-Z- is selected from $-CH_2-$, $-O-CH_2-$, $-CH_2-O-$, $-CH_2-CH_2-O-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$, wherein R18 is selected from:


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and

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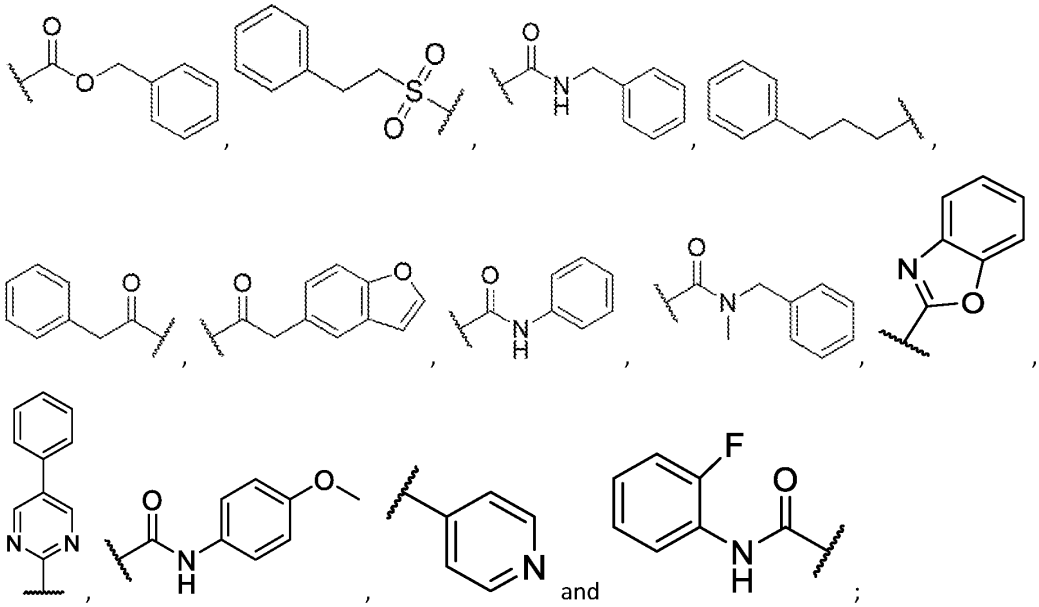
X is CR1R2; R1 is H; R2 is H; Y is O; and B is heteroaryl[a].

More preferably, -V-Z- is selected from $-CH_2-$, $-O-CH_2-$, $-CH_2-O-$, $-CH_2-CH_2-O-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$, wherein R18 is selected from:



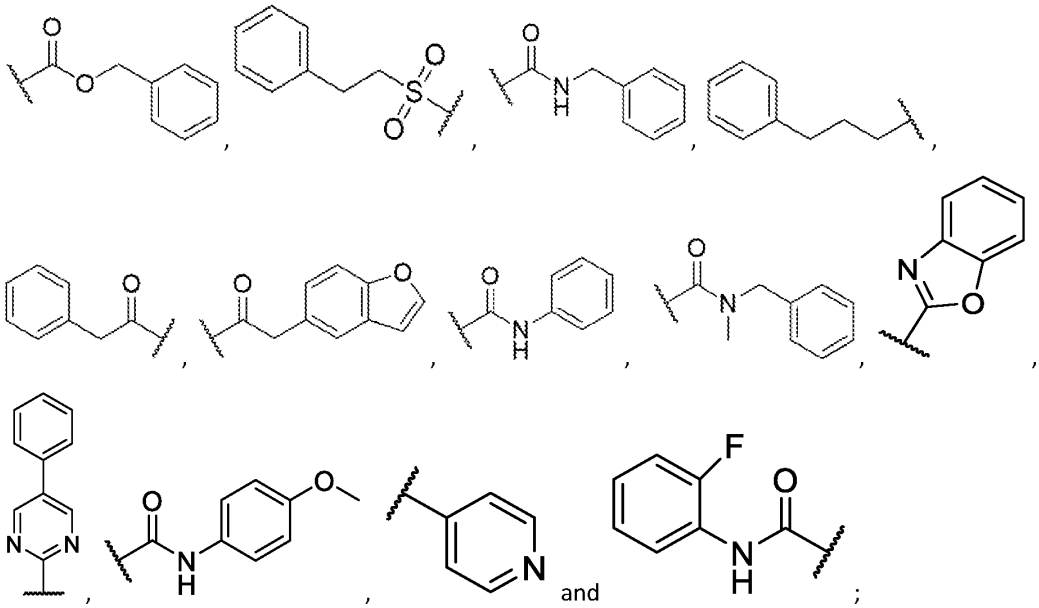
X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), optionally substituted as for heteroaryl[a].

Yet more preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



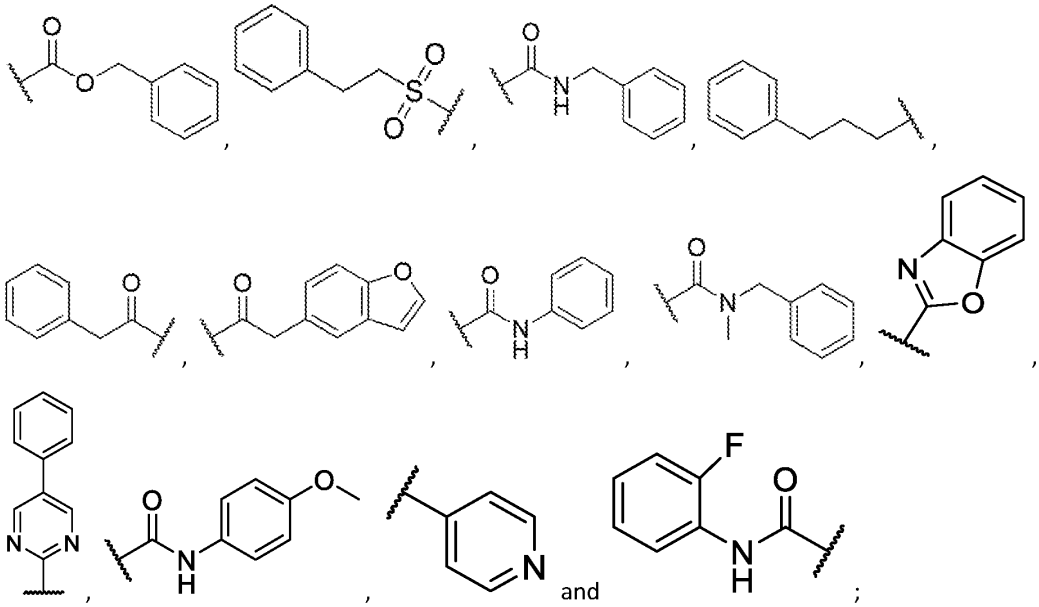
X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[b].

More specifically, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), optionally substituted as for heteroaryl[a].

Yet more preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[b].

More specifically, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-; X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

Preferably, X is CR1R2; R1 is H; R2 is H; Y is O; and B is heteroaryl[a]. More preferably, X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), optionally substituted as for heteroaryl[a]. Yet more preferably, X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with halo (e.g. chloro), and optionally substituted with 1 or 2 further substituents as for heteroaryl[a]. Alternatively, X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[b]. More specifically, X is CR1R2; R1 is H; R2 is H; Y is O; and B is azaindole (particularly 7-azaindole), substituted with NH_2 and halo (e.g. chloro), and optionally 1 further substituent as for heteroaryl[a].

AW- can be selected from:

-$(CH_2)_{0-6}$-(CHR15)-$(CH_2)_{0-6}$-A, -(CHR12)-A, -O-(CHR12)-A, -$(CH_2)_{0-6}$-A, -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A, -$(CH_2)_{0-6}$-NH-$(CH_2)_{0-6}$-A, -$(CH_2)_{0-6}$-NR12-$(CH_2)_{1-6}$-C(=O)-A, -$(CH_2)_{0-6}$-NH-C(=O)-$(CH_2)_{0-6}$-A, -C(=O)NR12-$(CH_2)_{0-6}$-A, -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A, -$(CH_2)_{0-6}$-(phenyl)-$(CH_2)_{0-6}$-A, -NH-SO_2-A and -SO_2-NH-A.

R15 is selected from alkyl, halo, CF_3, CN, OH, alkoxy, NR13R14, and CONR13R14. R15 can be alkyl (e.g. methyl or ethyl). R15 can be halo (e.g. fluoro or chloro). R15 can be CF_3. R15 can be CN. R15 can be OH. R15 can be alkoxy (e.g. methoxy or ethoxy). R15 can be NR13R14, particularly NH_2. R15 can be CONR13R14, particularly $CONH_2$.

AW- can be selected from:

-(CHR12)-A, -O-(CHR12)-A, -$(CH_2)_{0-5}$-A, -$(CH_2)_{0-5}$-O-$(CH_2)_{0-5}$-A, -$(CH_2)_{0-5}$-NH-$(CH_2)_{0-5}$-A,

$-(CH_2)_{0-5}$-NR12-$(CH_2)_{1-5}$-C(=O)-A, $-(CH_2)_{0-5}$-NH-C(=O)-$(CH_2)_{0-5}$-A, -C(=O)NR12-$(CH_2)_{0-5}$-A, $-(CH_2)_{0-5}$-C(=O)-$(CH_2)_{0-5}$-A, $-(CH_2)_{0-5}$-(phenyl)-$(CH_2)_{0-5}$-A, -NH-SO_2-A and -SO_2-NH-A.

AW- can be selected from:

-(CHR12)-A, -O-(CHR12)-A, $-(CH_2)_{0-4}$-A, $-(CH_2)_{0-4}$-O-$(CH_2)_{0-4}$-A, $-(CH_2)_{0-4}$-NH-$(CH_2)_{0-4}$-A, $-(CH_2)_{0-4}$-NR12-$(CH_2)_{1-4}$-C(=O)-A, $-(CH_2)_{0-4}$-NH-C(=O)-$(CH_2)_{0-4}$-A, -C(=O)NR12-$(CH_2)_{0-4}$-A, $-(CH_2)_{0-4}$-C(=O)-$(CH_2)_{0-4}$-A, $-(CH_2)_{0-4}$-(phenyl)-$(CH_2)_{0-4}$-A, -NH-SO_2-A and -SO_2-NH-A.

AW- can be selected from:

-(CHR12)-A, -O-(CHR12)-A, $-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A, $-(CH_2)_{0-3}$-NH-C(=O)-$(CH_2)_{0-3}$-A, -C(=O)NR12-$(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-(phenyl)-$(CH_2)_{0-3}$-A, -NH-SO_2-A and -SO_2-NH-A.

Preferably AW- can be selected from -(CHR12)-A, $-(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A, $-(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A, $-(CH_2)_{0-6}$-NH-$(CH_2)_{0-6}$-A, $-(CH_2)_{0-3}$-(phenyl)-$(CH_2)_{0-3}$-A and $-(CH_2)_{0-6}$-NH-C(=O)-$(CH_2)_{0-6}$-A. AW- can be selected from -(CHR12)-A, $-(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A, $-(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A, $-(CH_2)_{0-6}$-NH-$(CH_2)_{0-6}$-A, $-(CH_2)_{0-3}$-(phenyl)-$(CH_2)_{0-3}$-A and $-(CH_2)_{0-6}$-NH-C(=O)-$(CH_2)_{0-6}$-A.

Preferably, AW- can be selected from:

-O-(CHR12)-A, $-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A and -C(=O)NR12-$(CH_2)_{0-3}$-A.

More specifically, AW- can be selected from:

$-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and $-(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A.

Preferably AW- is selected from $-(CHR12)_{0-6}$-A and $-(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A. AW- can be selected from $-(CHR12)_{0-3}$-A and $-(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A.

Preferably AW- is selected from -(CHR12)-A, $-(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A, and $-(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A. AW- can be selected from $-(CHR12)_{0-3}$-A, $-(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A, and $-(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A.

Preferably AW- is selected from -(CHR12)-A and $-(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A. AW- can be selected from $-(CHR12)_{0-3}$-A and $-(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A.

Preferably AW- can be $-(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A.

Preferably AW- can be -CH_2-O-A.

AW- can be -(CHR12)-A. AW- can be -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A. AW- can be -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A. AW- can be -$(CH_2)_{0-6}$-NH-$(CH_2)_{0-6}$-A. AW- can be -$(CH_2)_{0-6}$-NH-C(=O)-$(CH_2)_{0-6}$-A. AW- can be -$(CH_2)_{0-3}$-(phenyl)-$(CH_2)_{0-3}$-A.

AW- can be -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A.

AW- can be -CH_2-O-A.

AW- can be -$(CHR12)_{0-6}$-A. AW- can be -$(CHR12)_{0-3}$-A. AW- can be –(CHR12)-A. AW- can be -$(CH_2)_{0-6}$-A. AW- can be -$(CH_2)_{0-3}$-A. AW- can be -(CH_2)-A.

AW- can be –(CHR12)-A. AW- can be -C(=O)-$(CH_2)_{0-6}$-A. AW- can be -$(CH_2)_{0-6}$-C(=O)-A. AW- can be -C(=O)-$(CH_2)_{0-3}$-A. AW- can be -$(CH_2)_{0-3}$-C(=O)-A. AW- can be -C(=O)-A. AW- can be -$(CH_2)_{0-6}$-A. AW- can be -$(CH_2)_{0-3}$-A. AW- can be -(CH_2)-A.

AW- can be –(CHR12)-A. AW- can be -$(CH_2)_{0-6}$-A. AW- can be -$(CH_2)_{0-3}$-A. AW- can be -(CH_2)-A.

AW- can be -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A. AW- can be -$(CH_2)_{0-3}$-O-$(CH_2)_{0-6}$-A. AW- can be -$(CH_2)_{0-6}$-O-$(CH_2)_{0-3}$-A. AW- can be -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A. AW can be -(CH_2)-O-$(CH_2)_{0-6}$-A. AW- can be -$(CH_2)_{0-6}$-O-A. AW can be -$(CH_2)_{0-6}$-O-(CH_2) –A. AW can be -O-$(CH_2)_{0-6}$-A. AW- can be -$(CH_2)_{0-3}$-O-A. AW- can be -O-$(CH_2)_{0-3}$-A. AW- can be -(CH_2)-O-(CH_2)-A. AW- can be -O-(CH_2)-A. Preferably AW- is -(CH_2)-O-A.

AW- can be -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A. AW- can be -$(CH_2)_{0-3}$-O-$(CH_2)_{0-6}$-A. AW- can be -$(CH_2)_{0-6}$-O-$(CH_2)_{0-3}$-A. AW- can be -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A. AW- can be -$(CH_2)_{0-6}$-O-A. AW can be -O-$(CH_2)_{0-6}$-A. AW- can be -$(CH_2)_{0-3}$-O-A. AW- can be -O-$(CH_2)_{0-3}$-A. AW- can be -(CH_2)-O-(CH_2)-A. AW- can be -O-(CH_2)-A. Preferably AW- is -(CH_2)-O-A.

A can be a 4- to 15- membered mono-, bi-, or tri- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein when A is a bicyclic ring system, the bicyclic ring

system is fused, bridged or spiro; wherein when A is a tricyclic ring system, each of the three rings in the tricyclic ring system is either fused, bridged or spiro to at least one of the other rings in the tricyclic ring system.

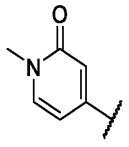
A can be a 4- to 15- membered mono-, bi-, or tri- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro; wherein when A is a tricyclic ring system, each of the three rings in the tricyclic ring system is either fused, bridged or spiro to at least one of the other rings in the tricyclic ring system.

A can be a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro.

A can be a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro. A can be a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl; wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro. A can be a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one further ring member independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl; wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro.

A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one further ring member independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl.

A can be a 6- membered monocyclic ring system containing one N ring member, wherein the ring system is substituted with 1 substituent selected from alkyl and cycloalkyl. More preferably, A is a 6-membered monocyclic ring system containing one N ring member, wherein the ring system is substituted with 1 alkyl substituent selected from methyl, ethyl, iso-propyl and cyclopropyl. Preferably, the 6-membered monocyclic ring system containing one N ring member is joined to W at the carbon para to the nitrogen.

A can be a 6- membered monocyclic ring system containing one N ring member and optionally one further ring member selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. Preferably, A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. More preferably, A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1 or 2 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. Most preferably, A is a 6-membered monocyclic ring system containing one N ring member, wherein the ring system is substituted with 2 substituents independently selected from alkyl and oxo. For example, A can be 

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A can be a 4- to 12- membered bicyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN;
wherein the bicyclic ring system is fused, bridged or spiro.

A can be a 6- to 12- membered bicyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN;
wherein the bicyclic ring system is fused, bridged or spiro.

A can be a fused 6- to 12- membered bicyclic ring system containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, wherein the fused ring system consists of an aromatic ring fused to a non-aromatic ring, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. A can be a fused 6- to 12- membered bicyclic ring system containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, wherein the fused ring system consists of an aromatic ring fused to a non-aromatic ring, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and CF_3.

A can be a fused 6- to 12- membered bicyclic ring system containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, wherein the fused ring system consists of a 5-membered aromatic ring fused to a 6-membered non-aromatic ring, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. A can be a fused 6- to 12- membered bicyclic ring system containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, wherein the fused ring system consists of a 5-membered aromatic ring fused to a 6-membered non-aromatic ring, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and CF_3.

A can be a 9- or 10- membered bicyclic ring system (particularly 9-membered), containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein the bicyclic ring system is fused, bridged or spiro.

A can be a fused 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, wherein the fused ring system consists of an aromatic ring fused to a non-aromatic ring, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. A can be a fused 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, wherein the fused ring system consists of an aromatic ring fused to a non-aromatic ring, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and CF_3.

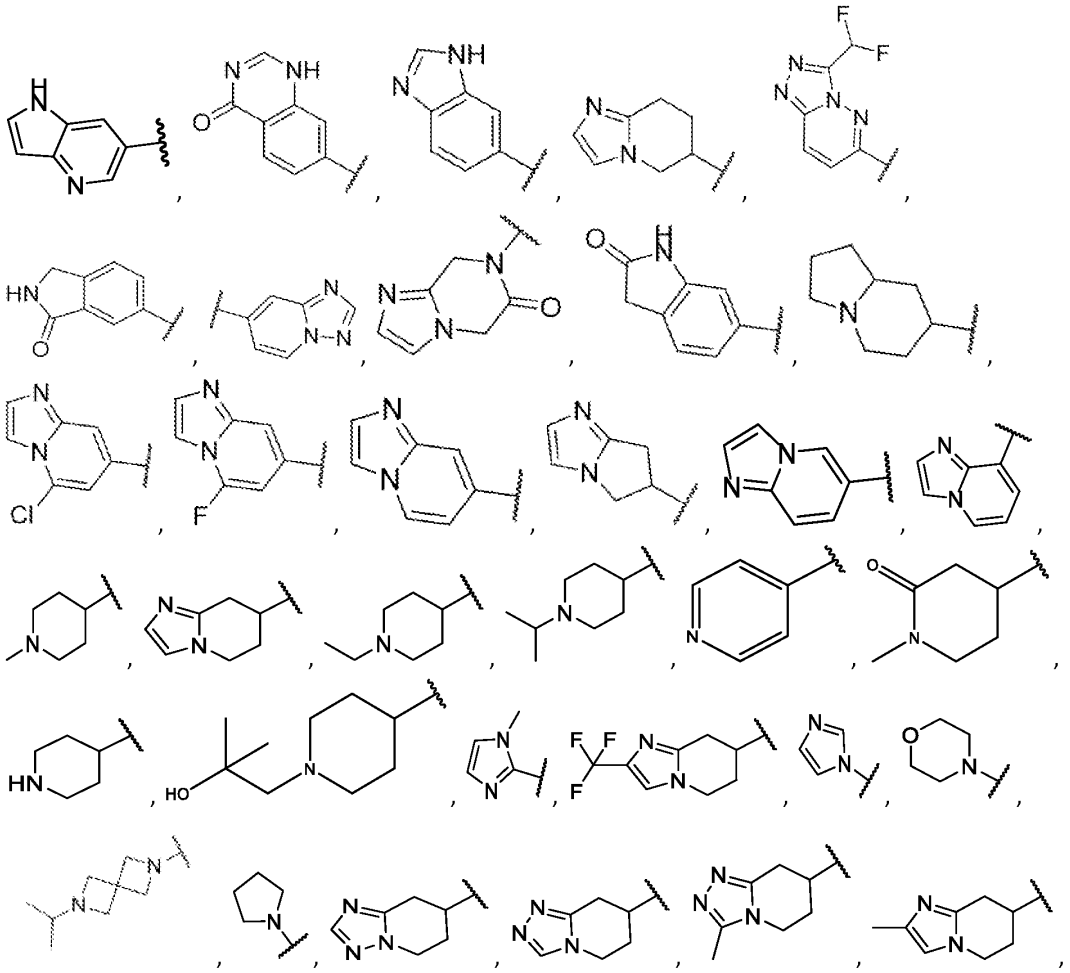
A can be a fused 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, wherein the fused ring system consists of a 5-membered aromatic ring fused to a 6-membered non-aromatic ring, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. A can be a fused 9- or 10-membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, wherein the fused ring system consists of a 5-membered aromatic ring fused to a 6-membered non-aromatic ring, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and CF_3.

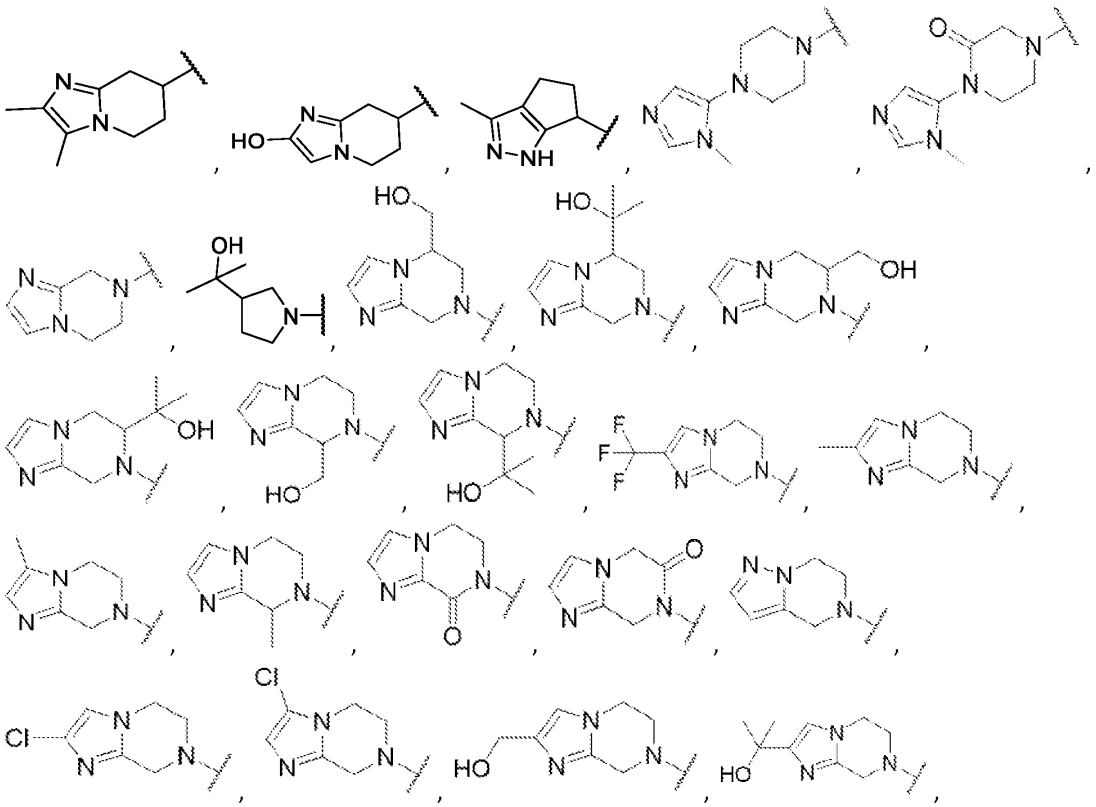
A can be a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12,

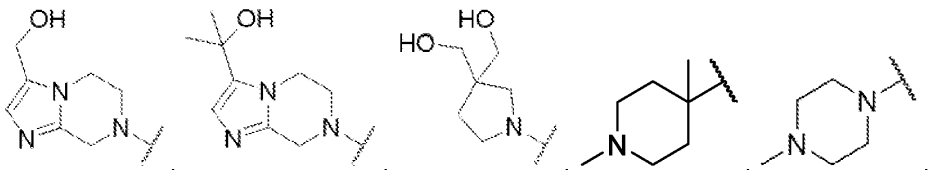
C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. One of the rings in the fused bicyclic ring system can be aromatic. Both of the rings in the fused bicyclic ring system can be aromatic.

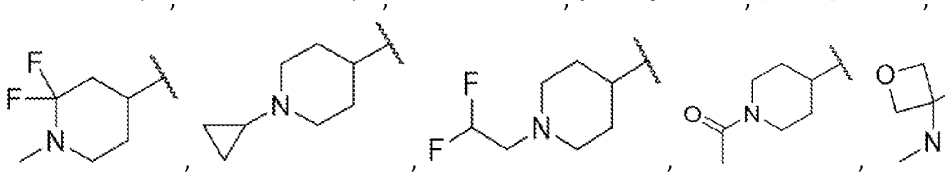
A can be a fused 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. One of the rings in the fused bicyclic ring system can be aromatic. Both of the rings in the fused bicyclic ring system can be aromatic.

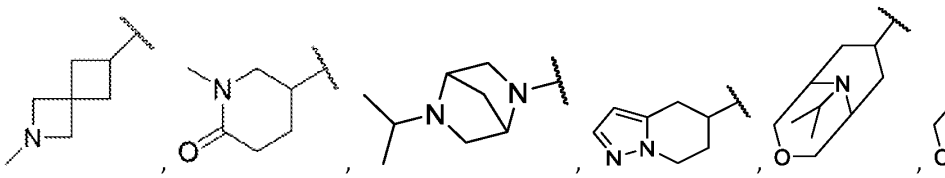
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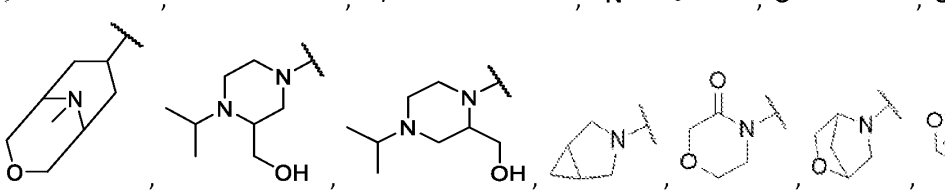


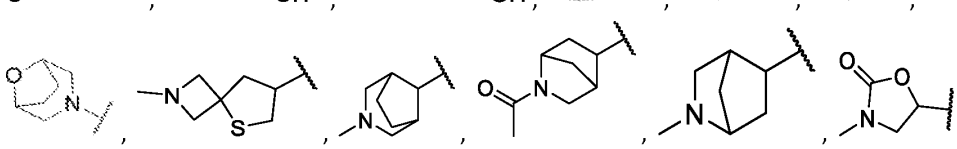


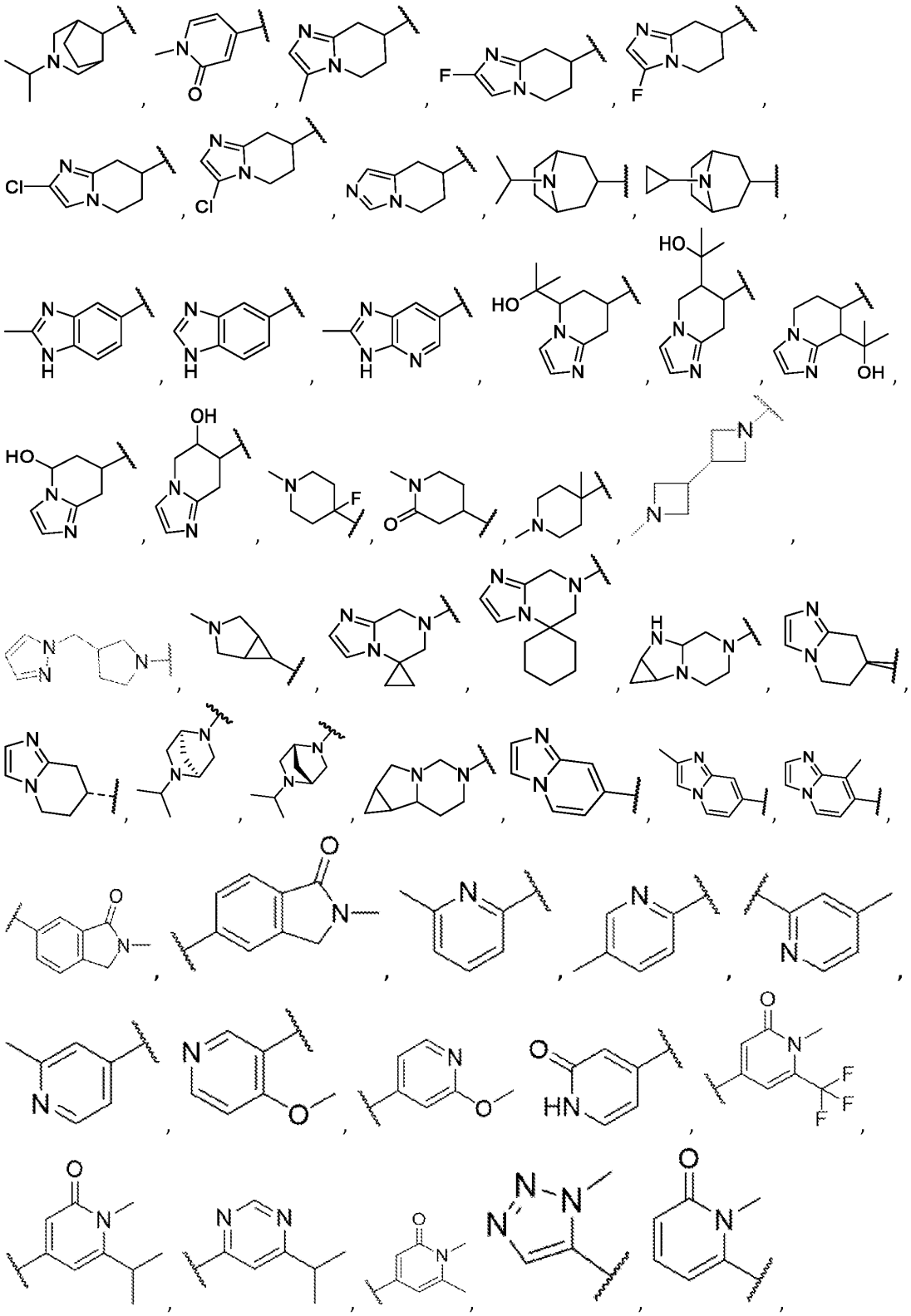


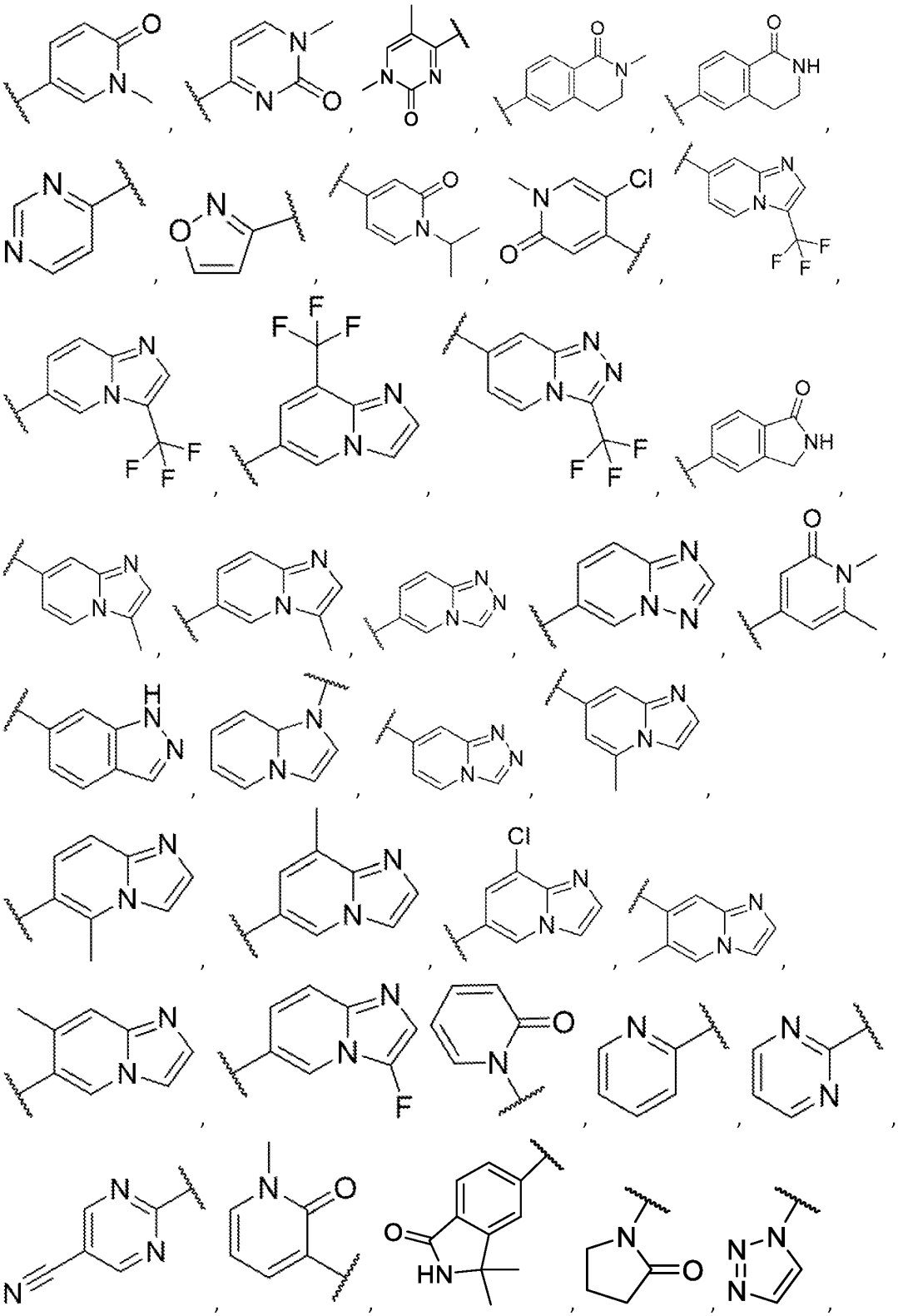


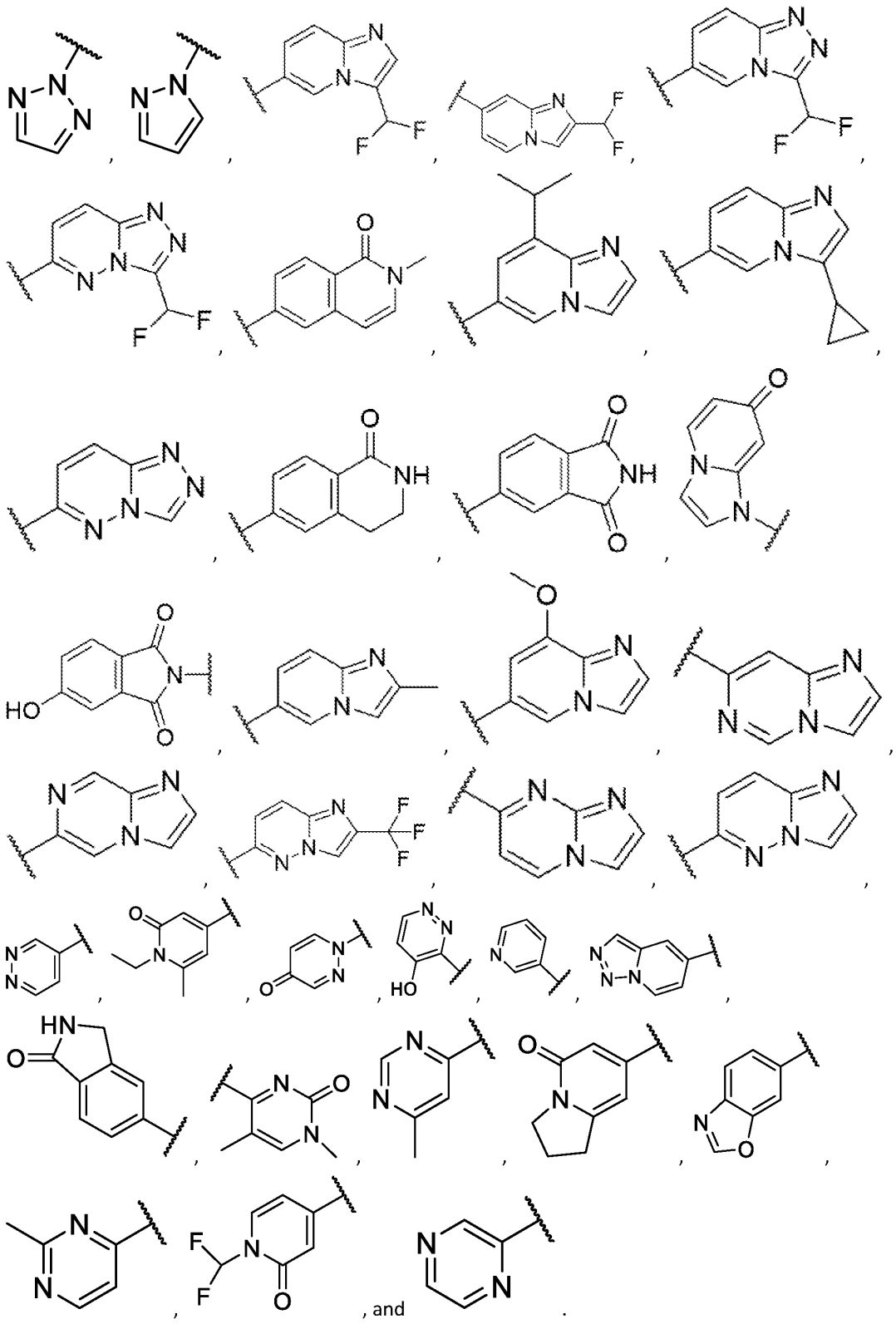






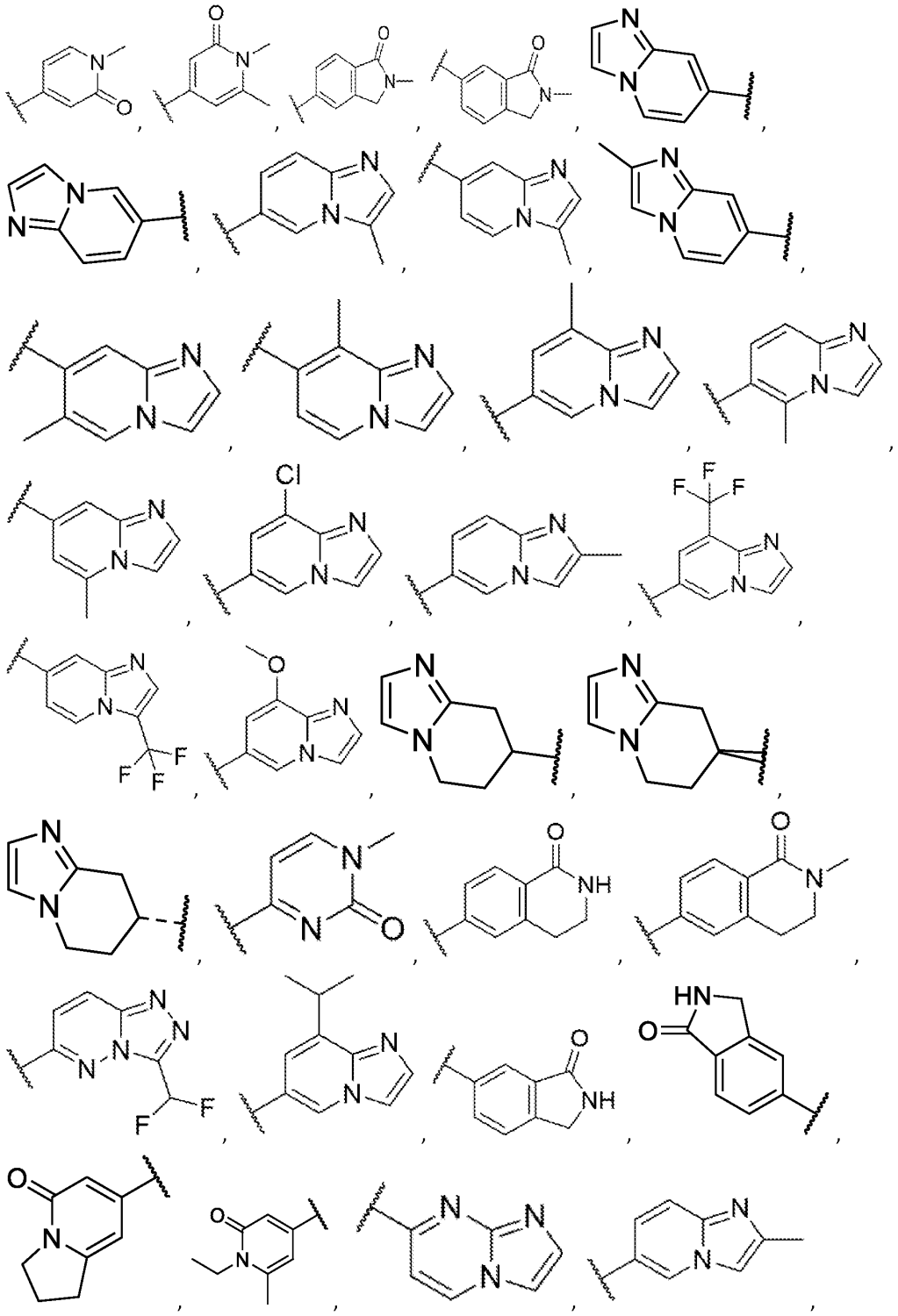


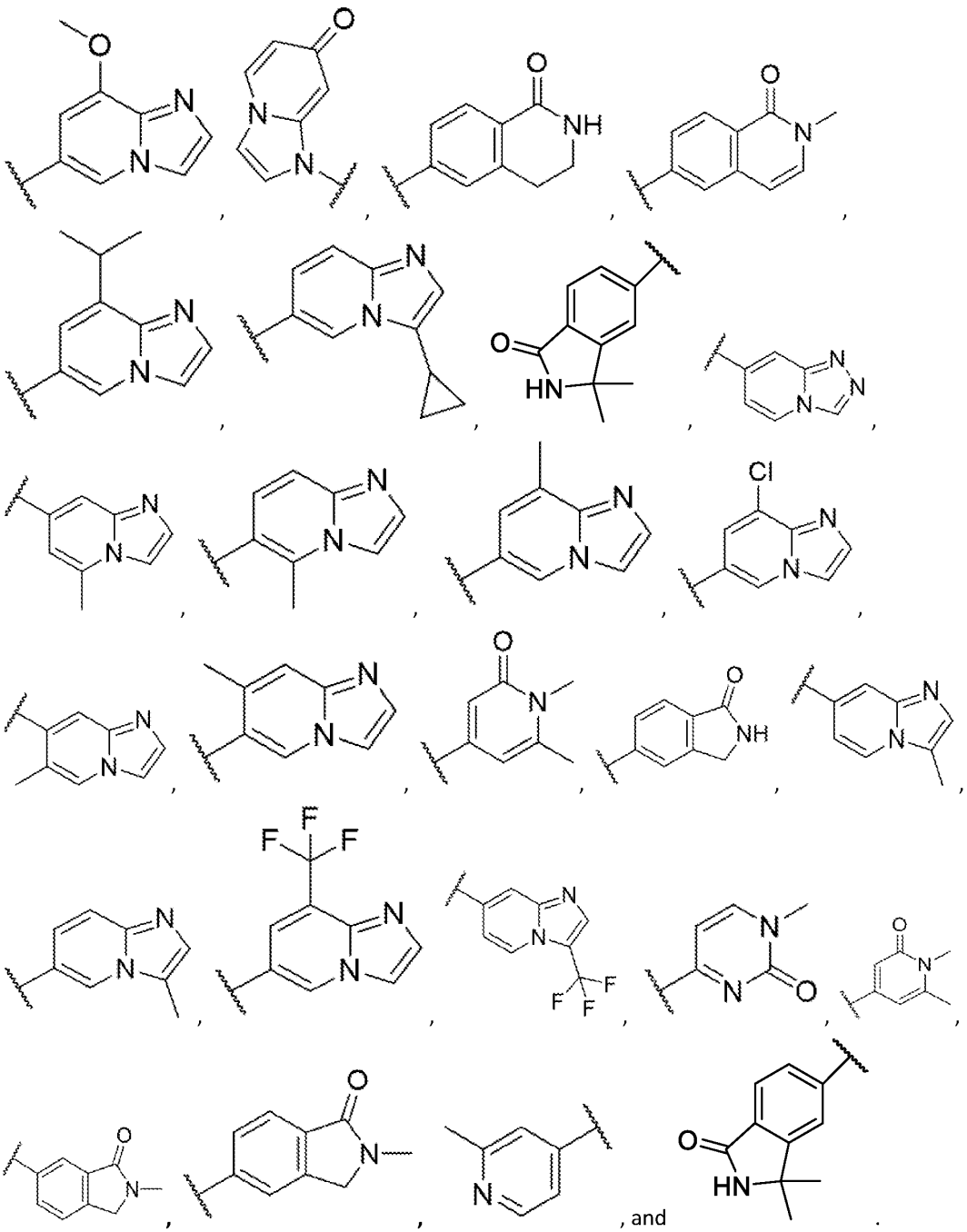




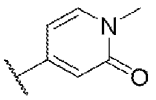
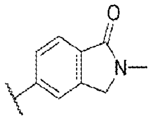
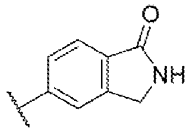
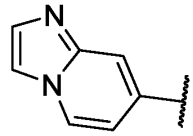
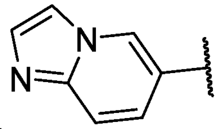
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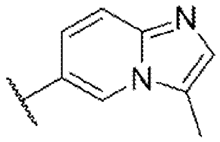
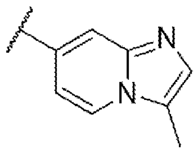
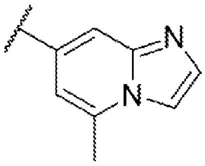
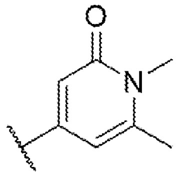
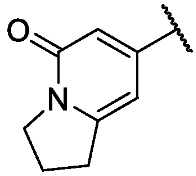
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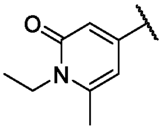
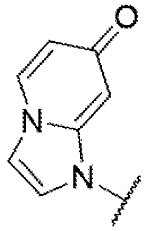
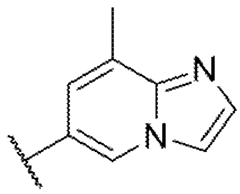
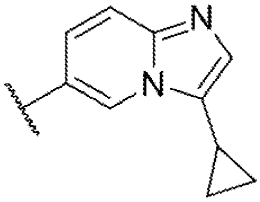


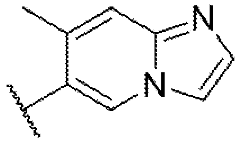
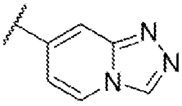
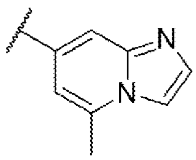
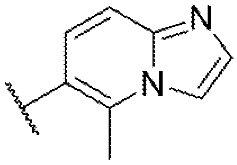


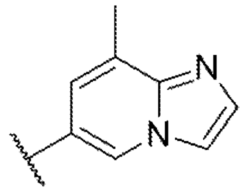
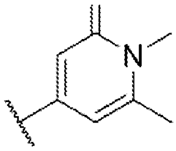
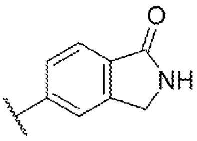
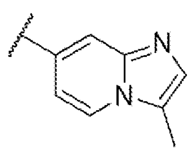
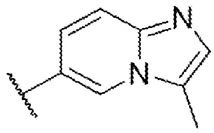
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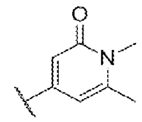
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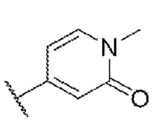
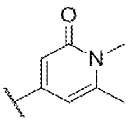
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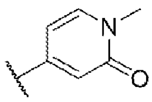
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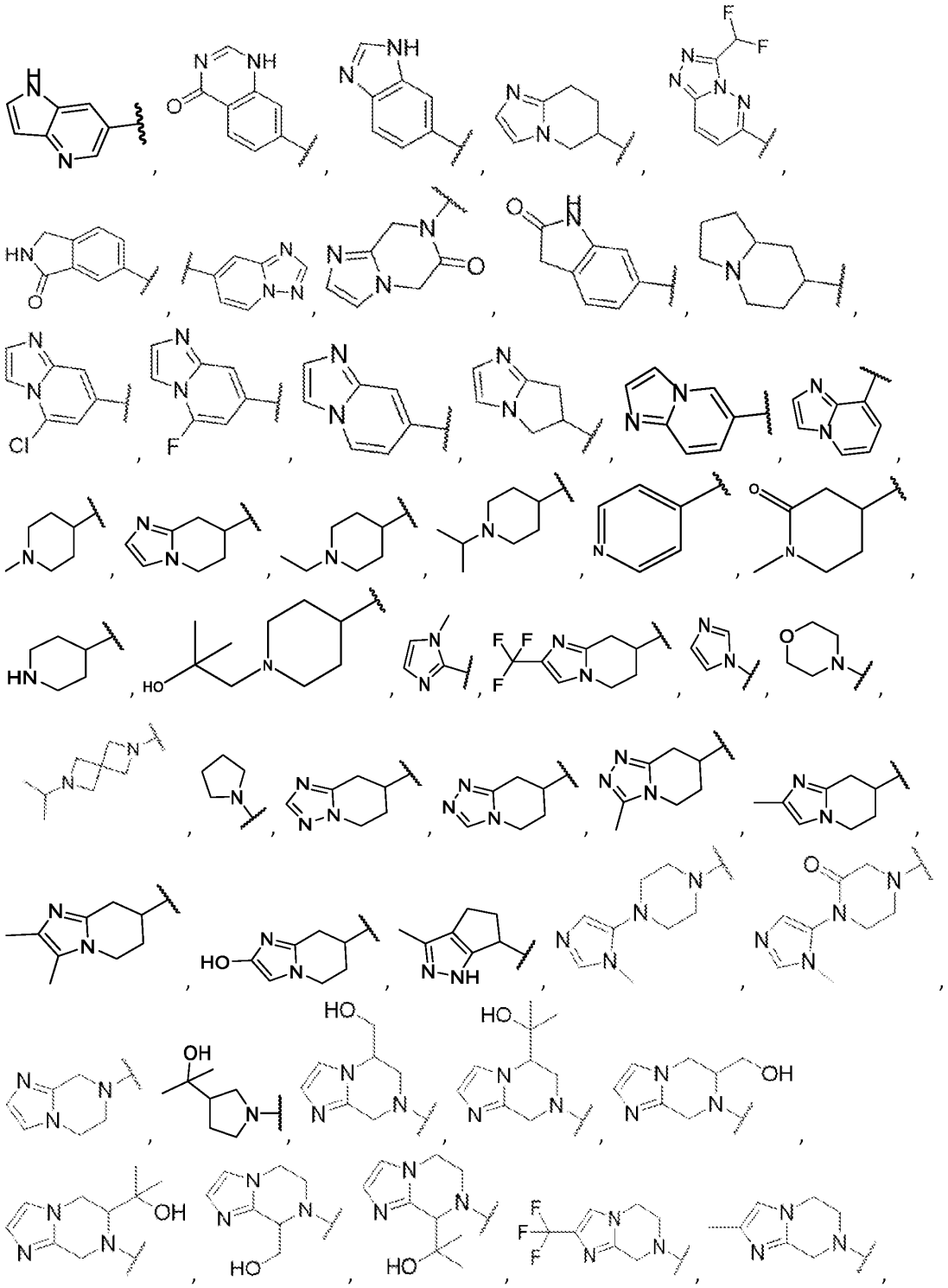
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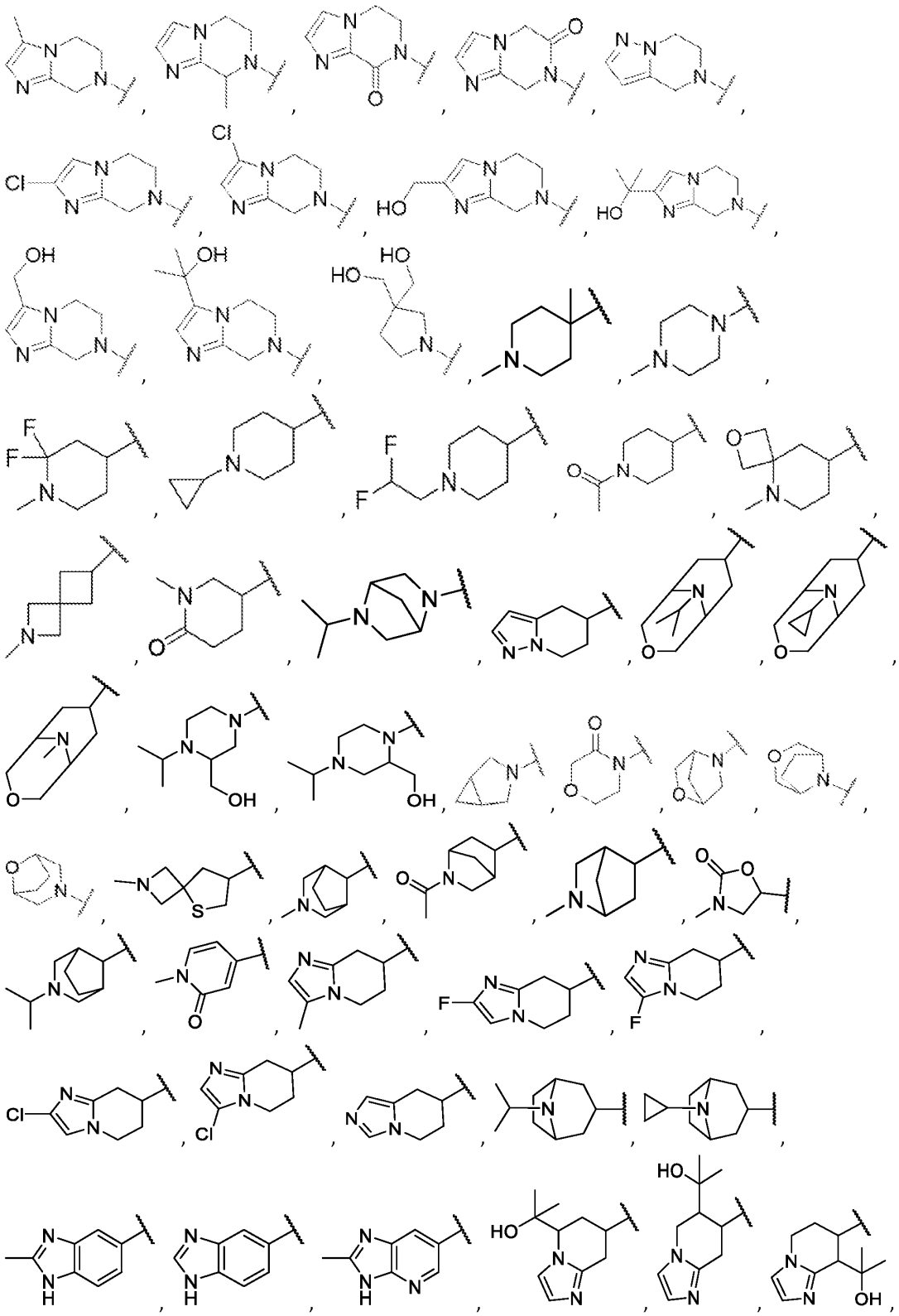
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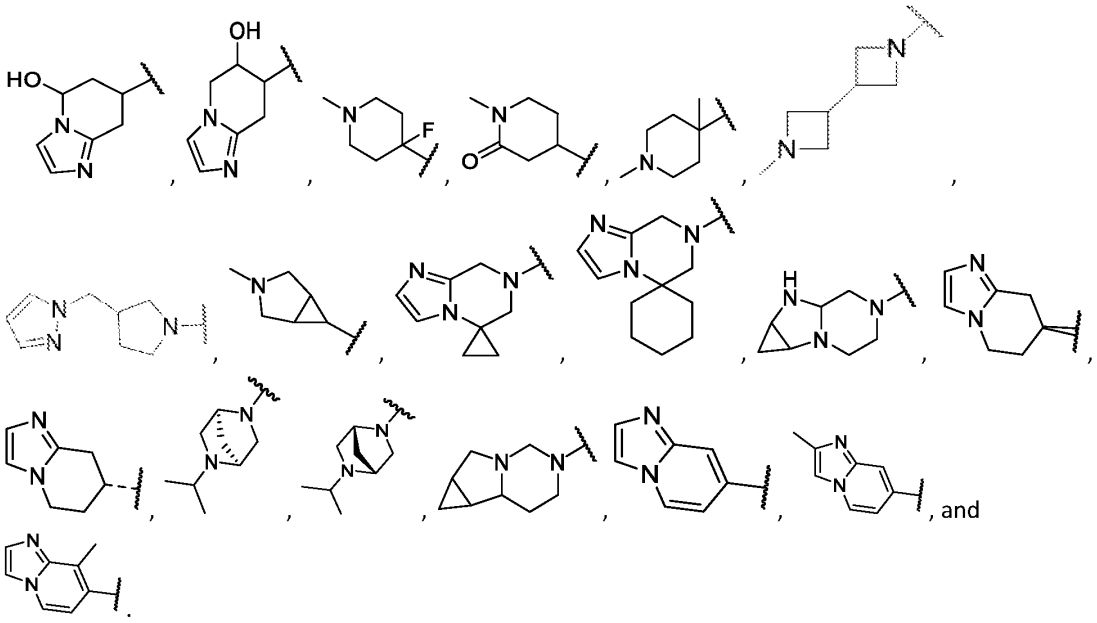
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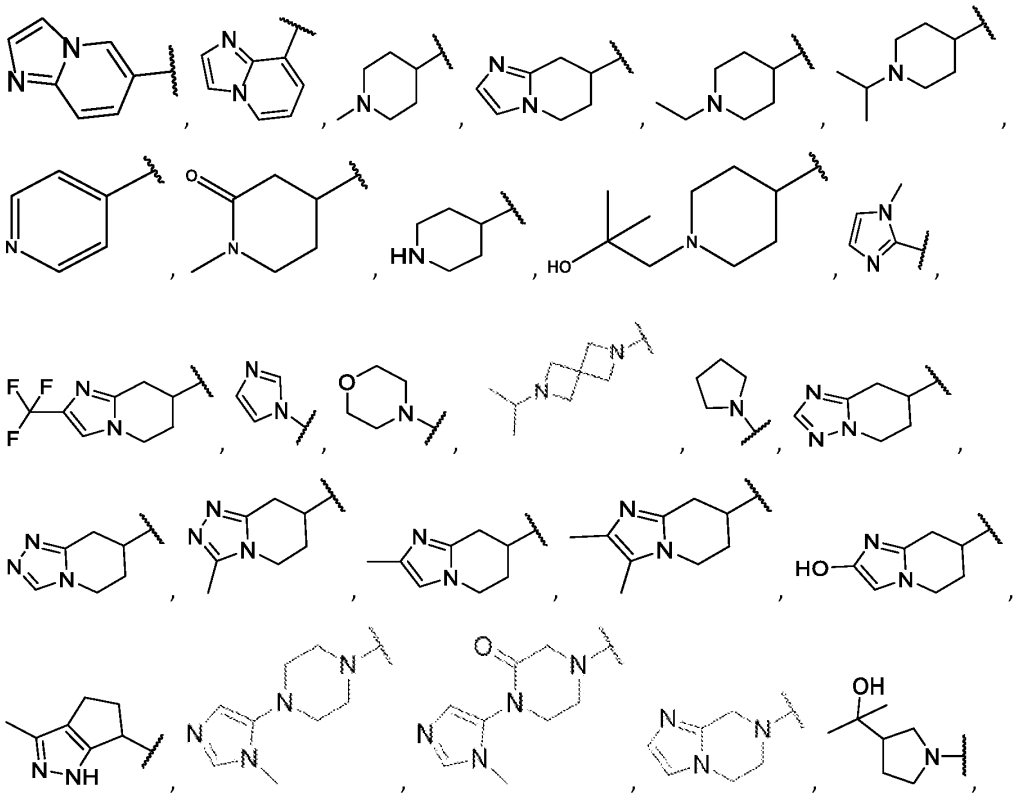
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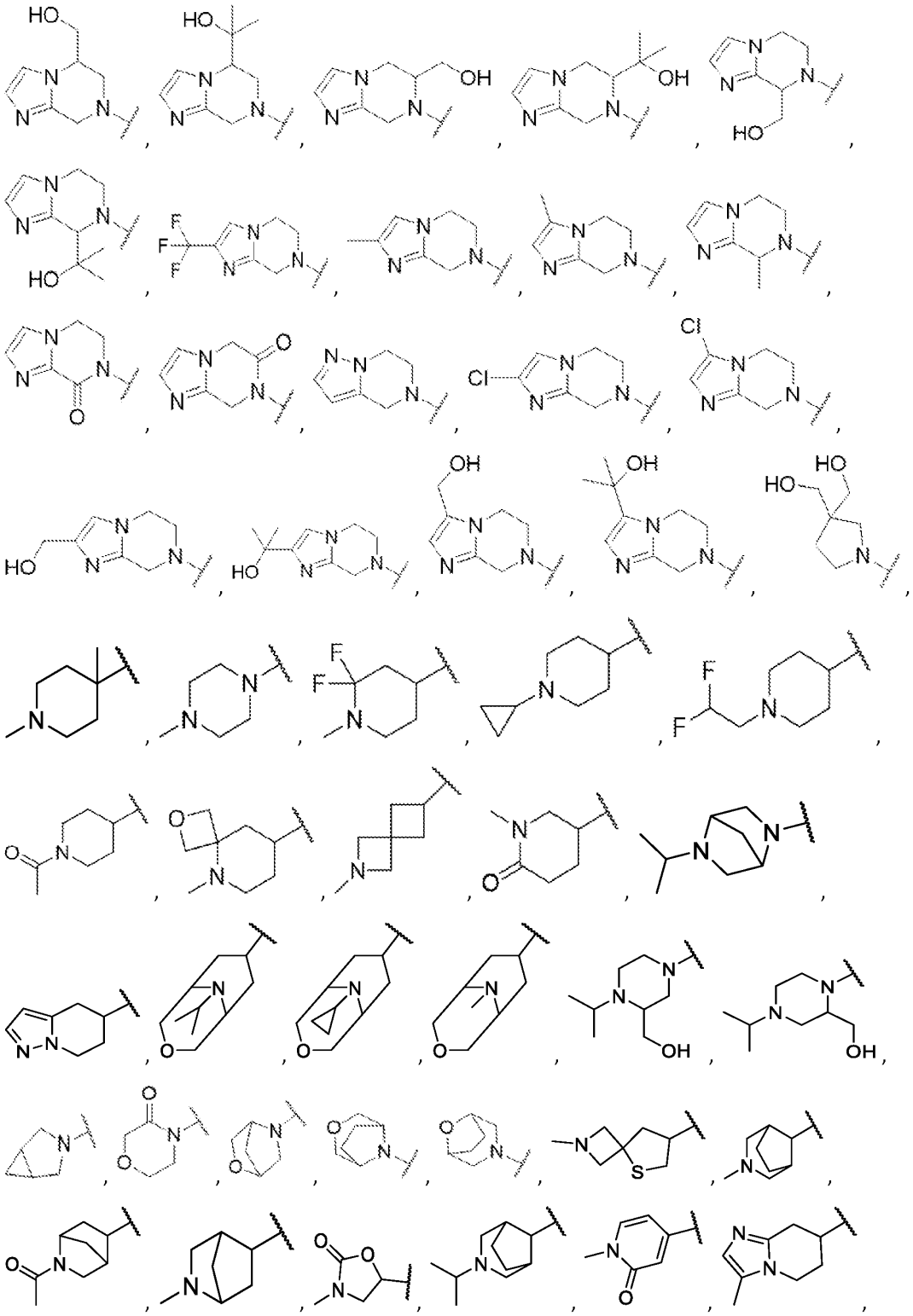


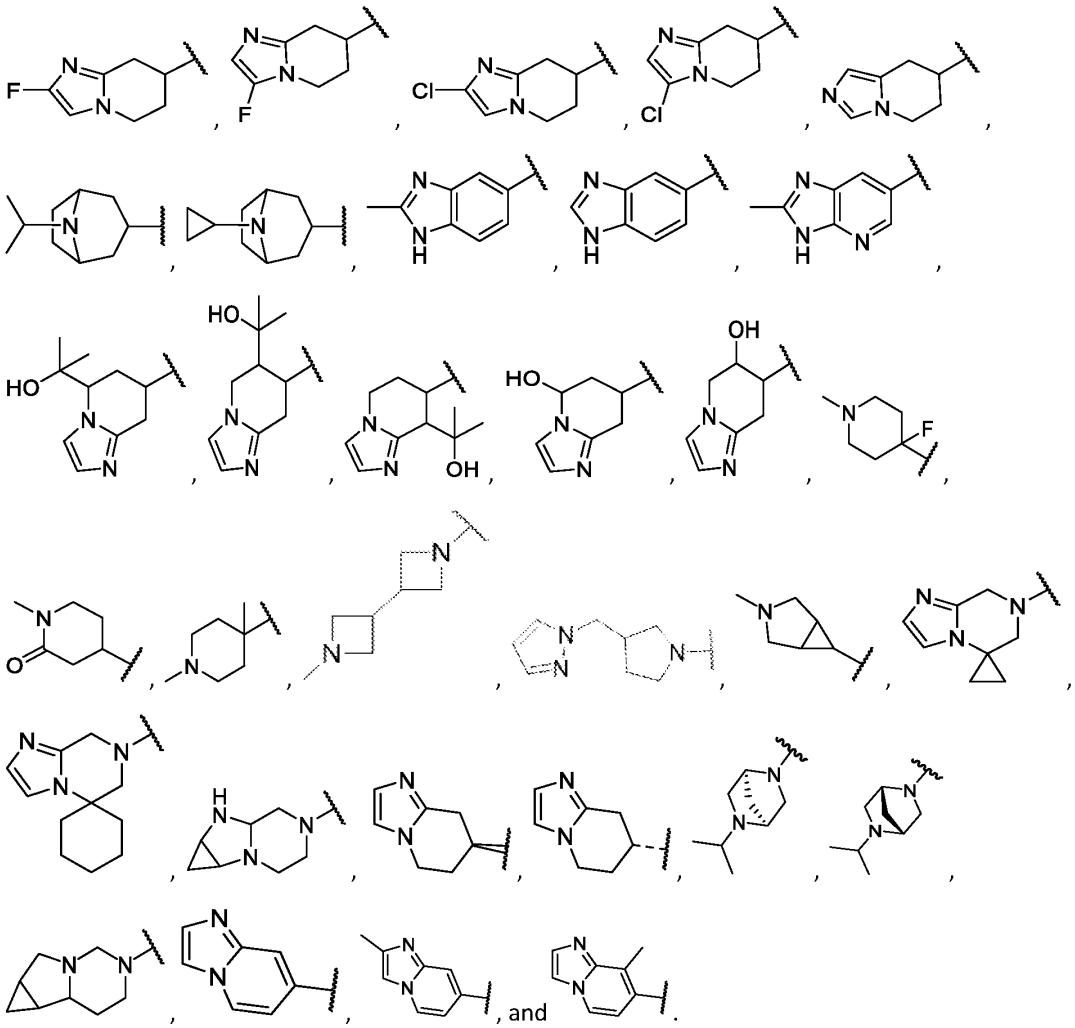




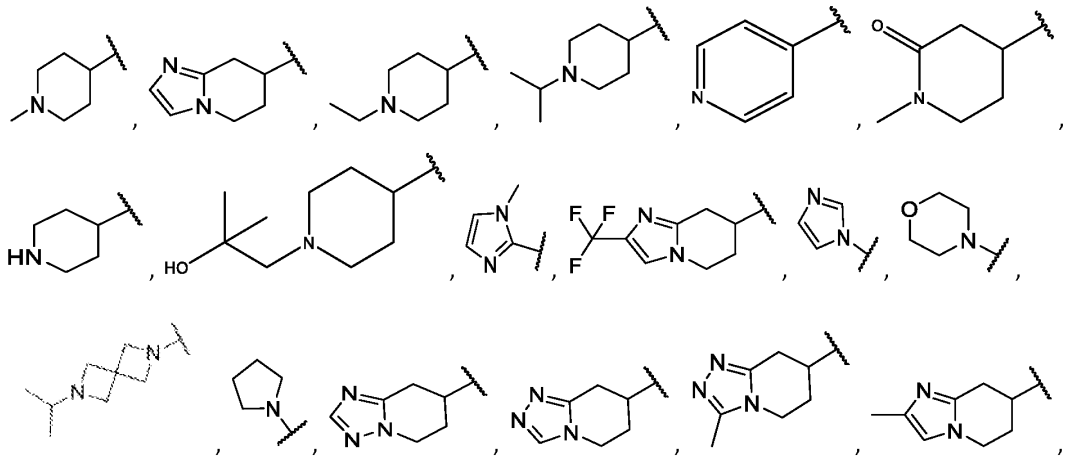
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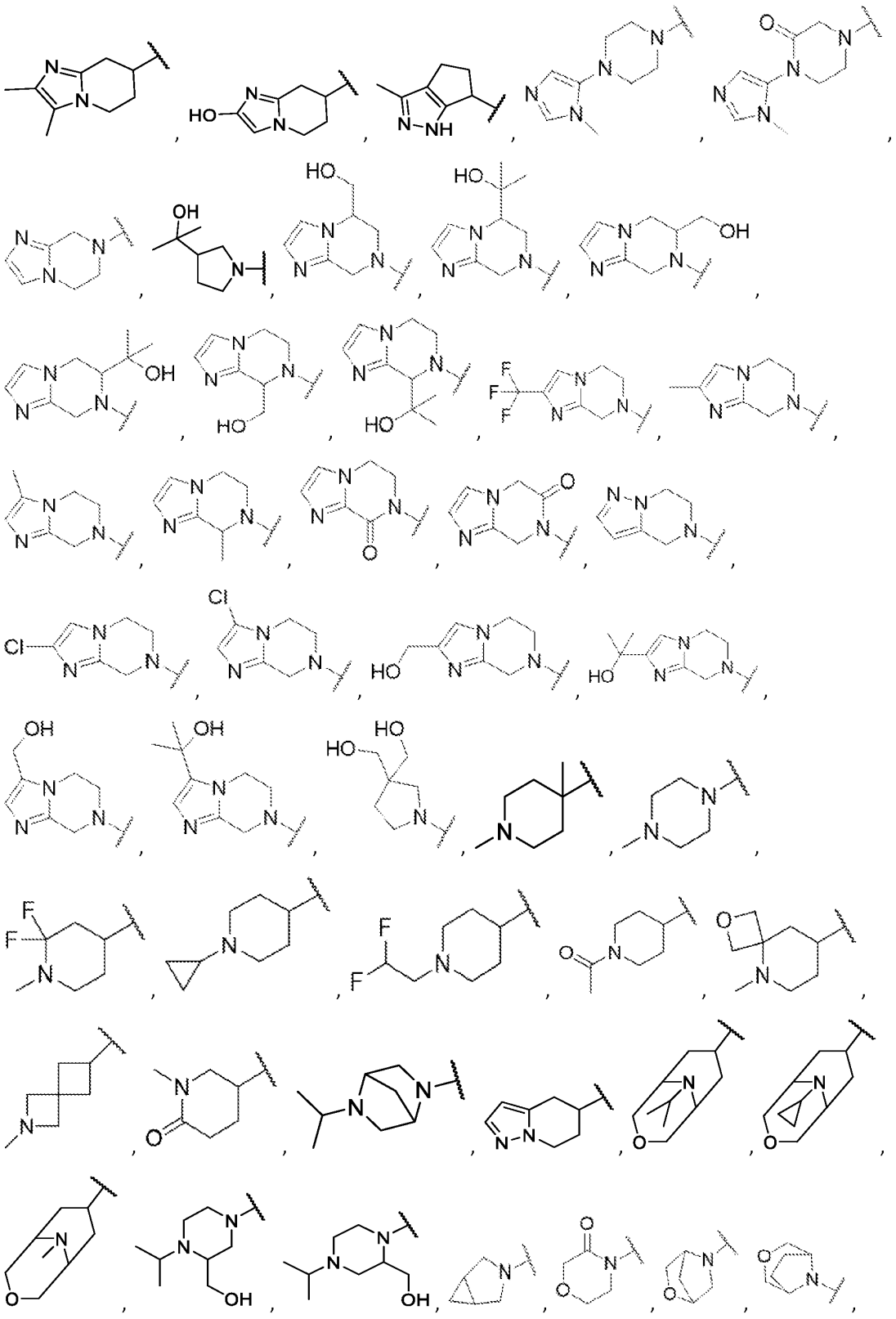


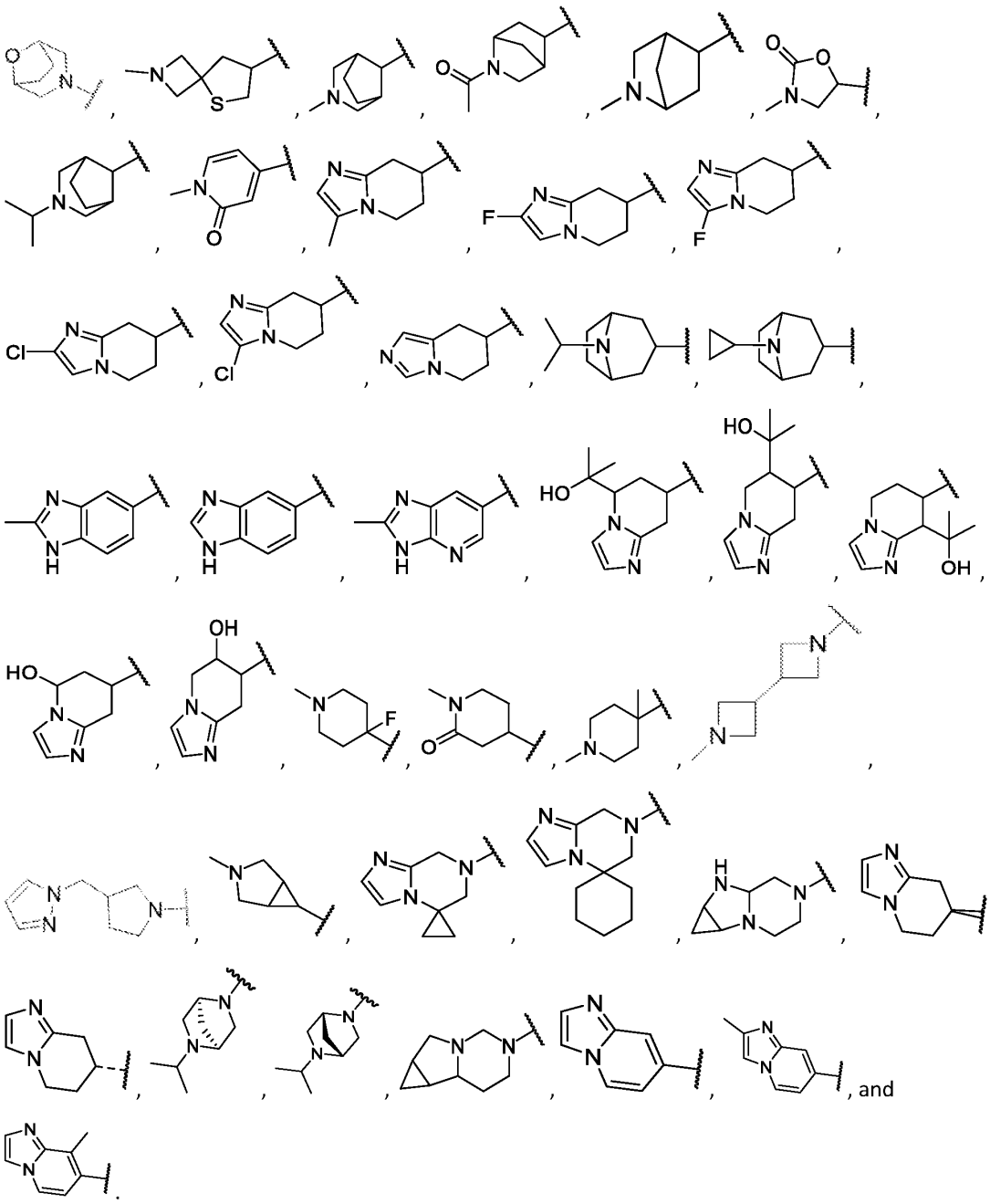




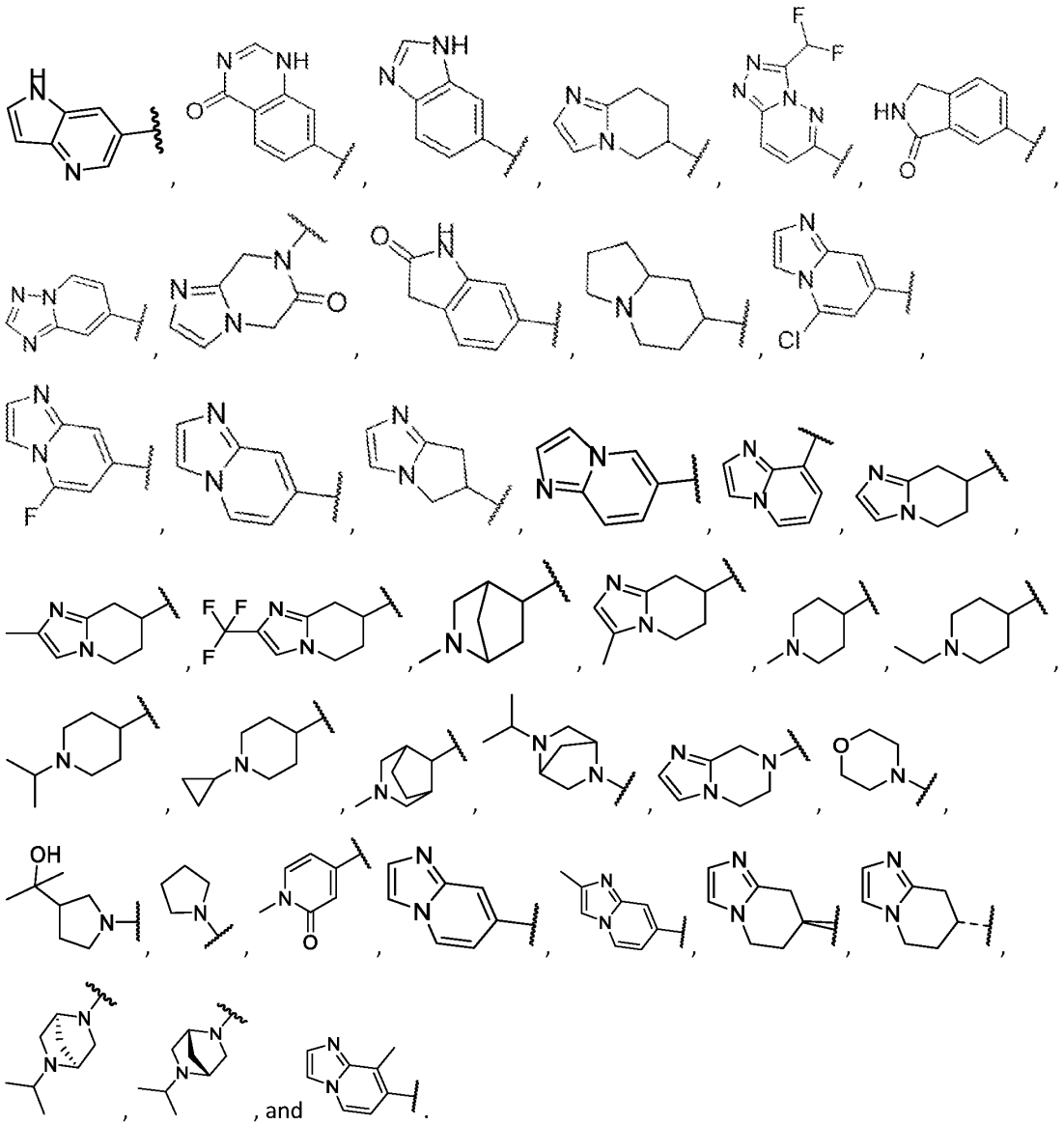
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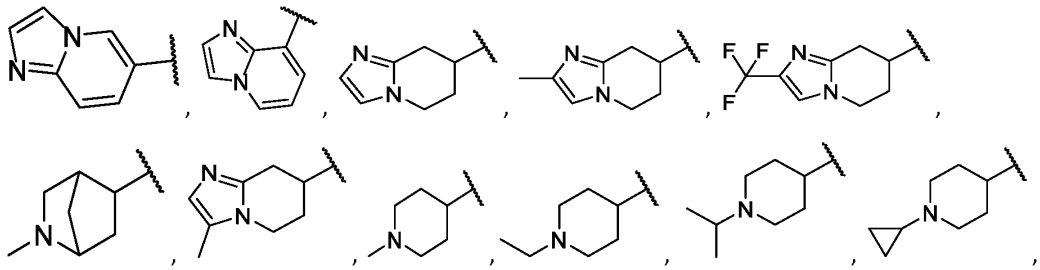


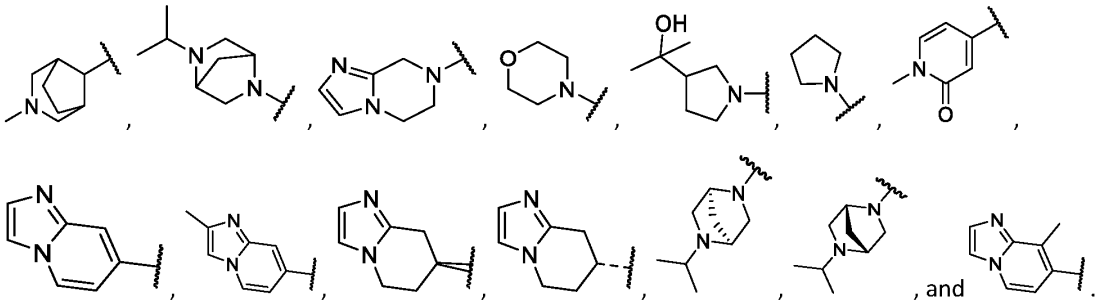


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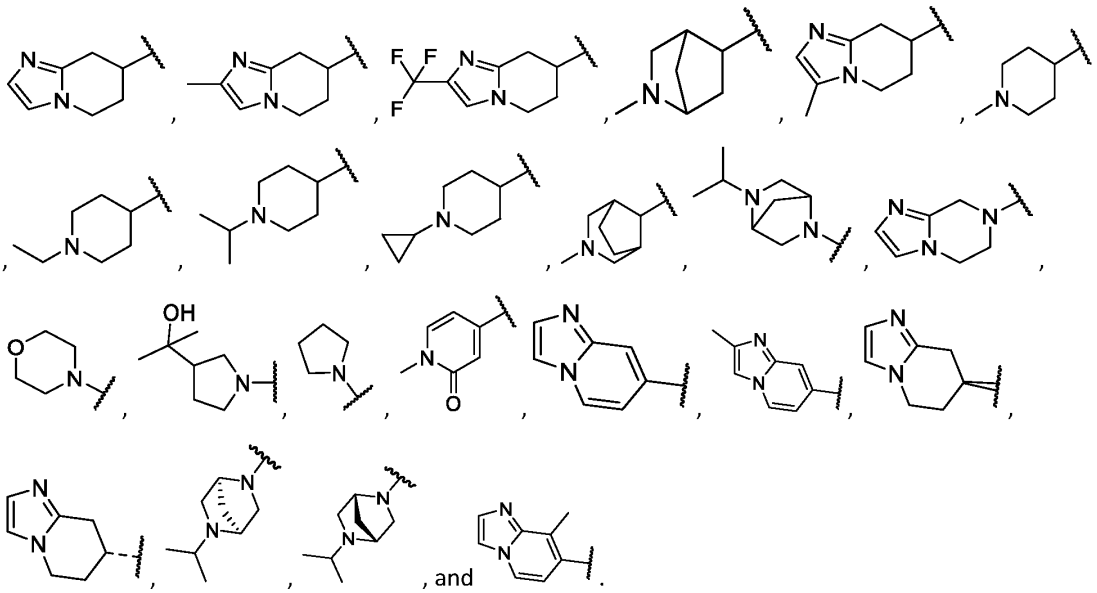


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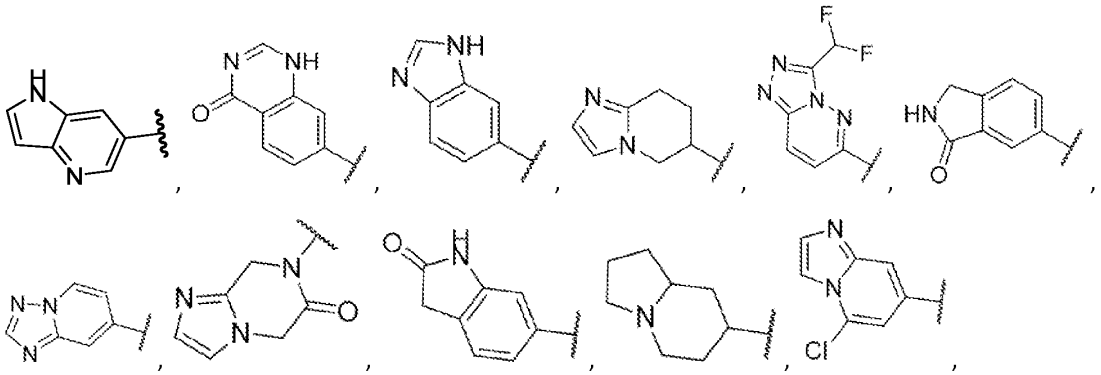


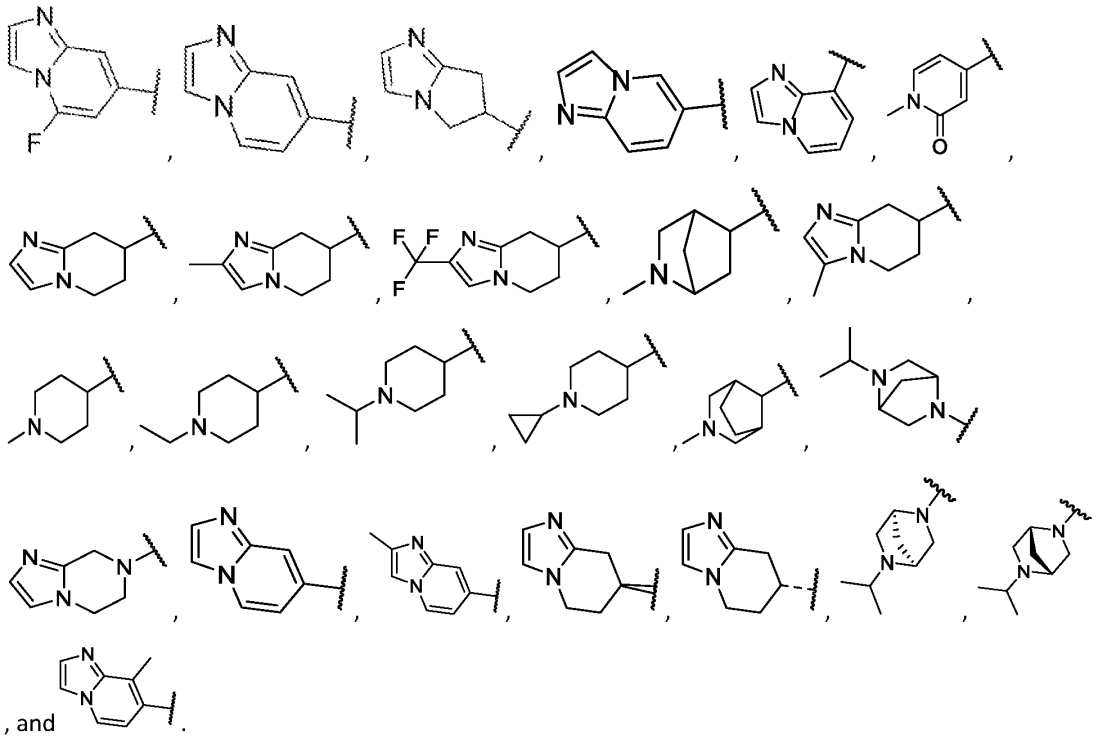


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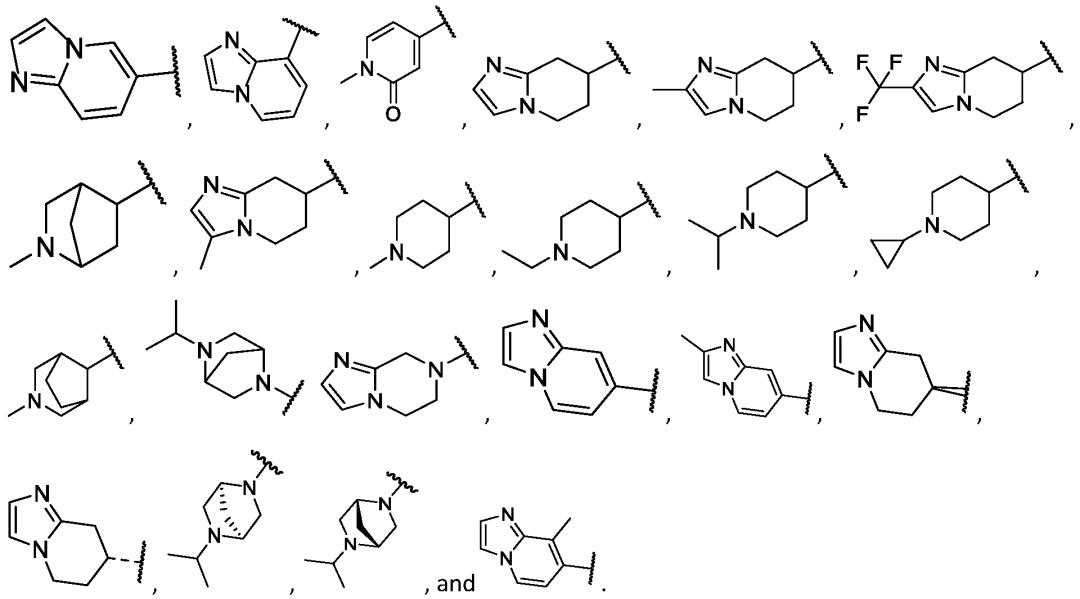


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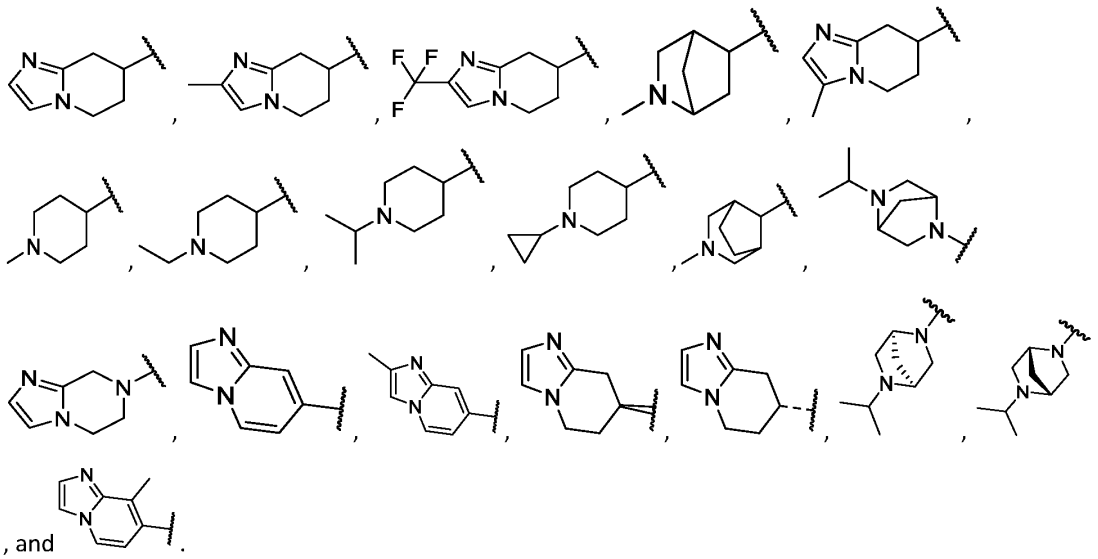




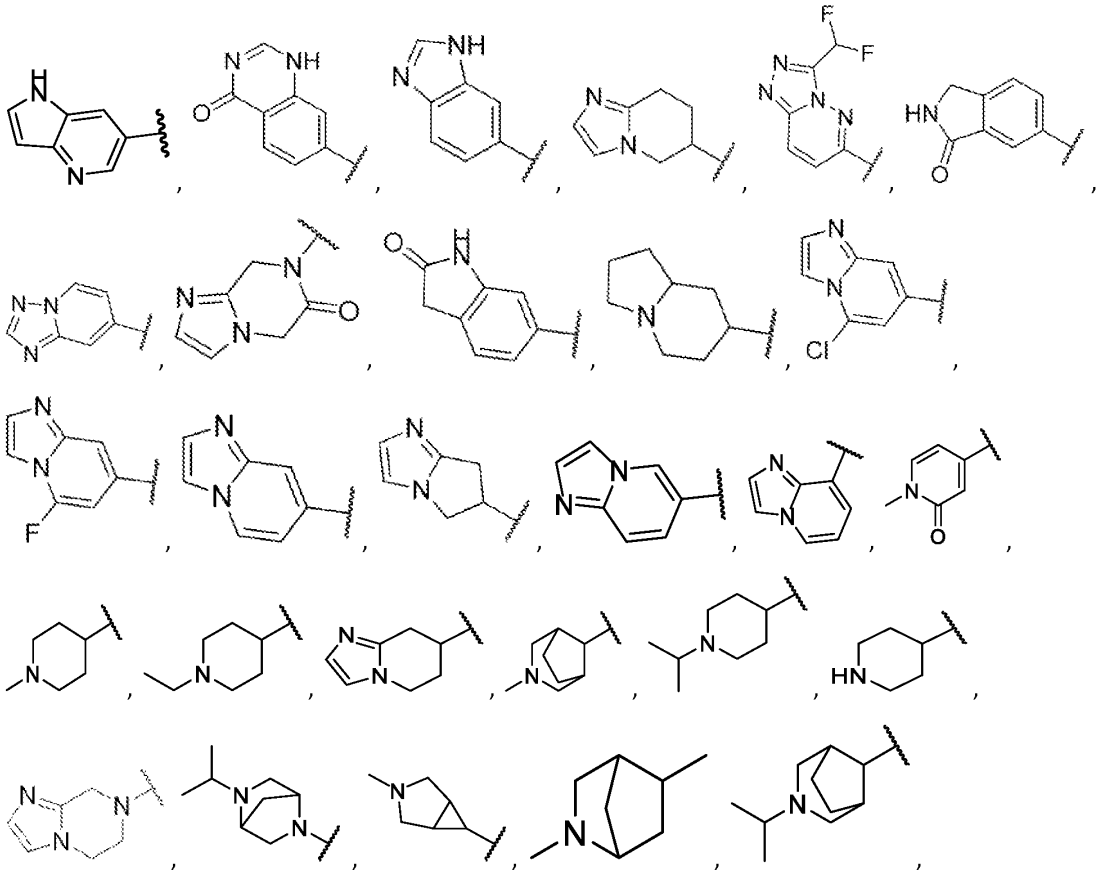
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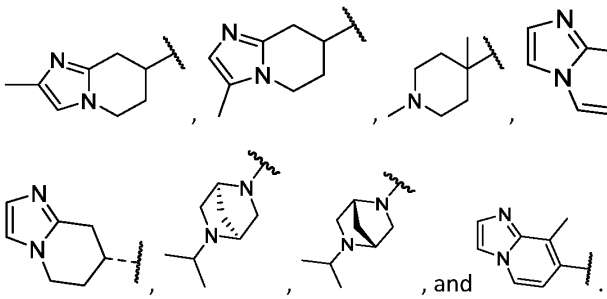


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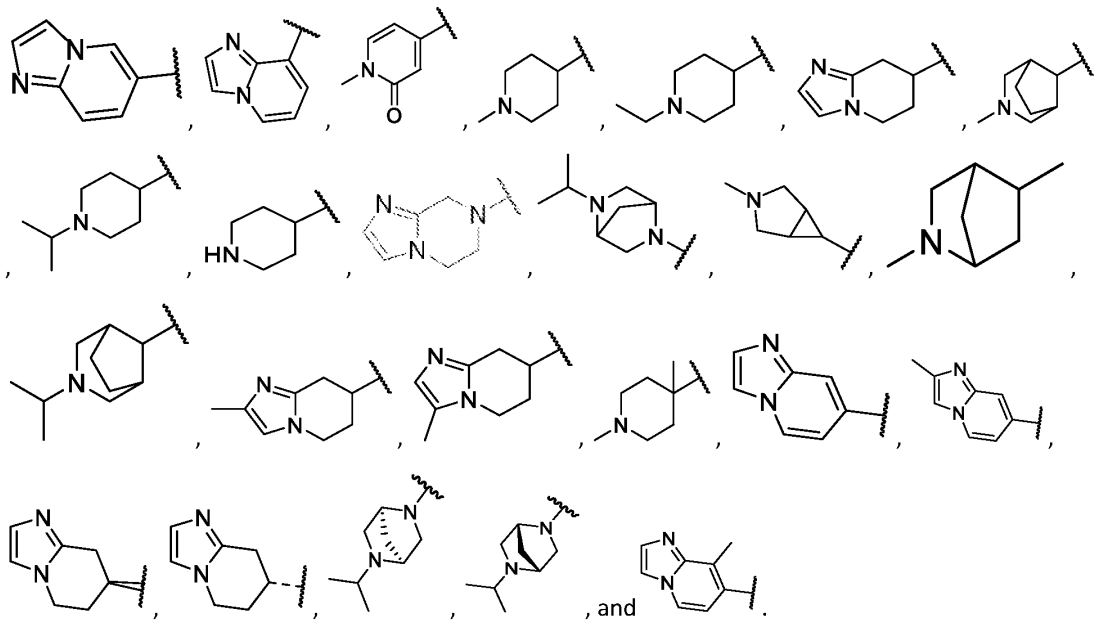

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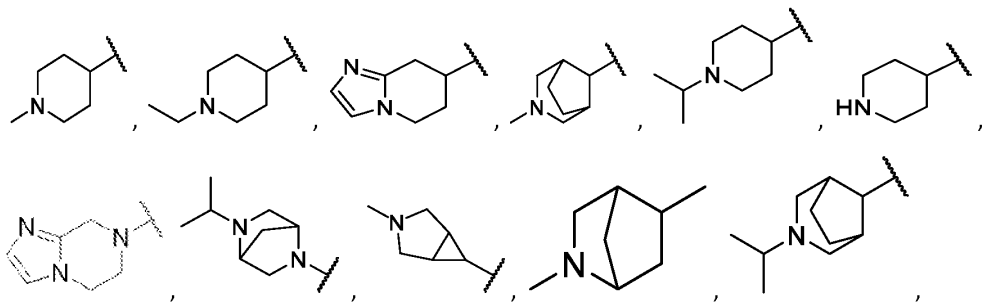


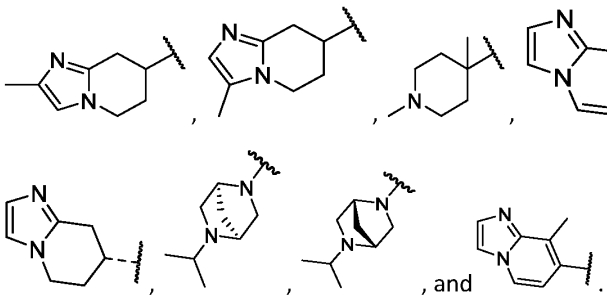


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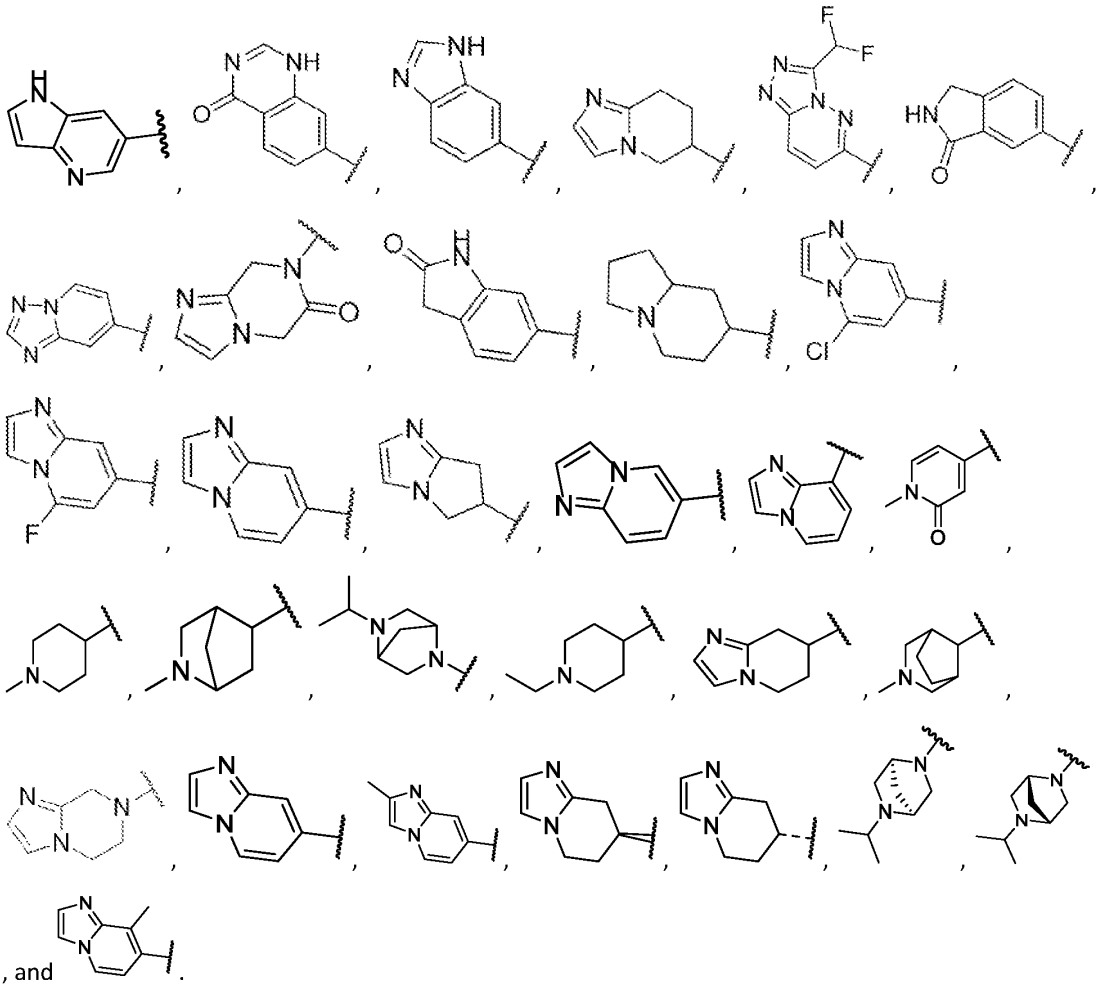


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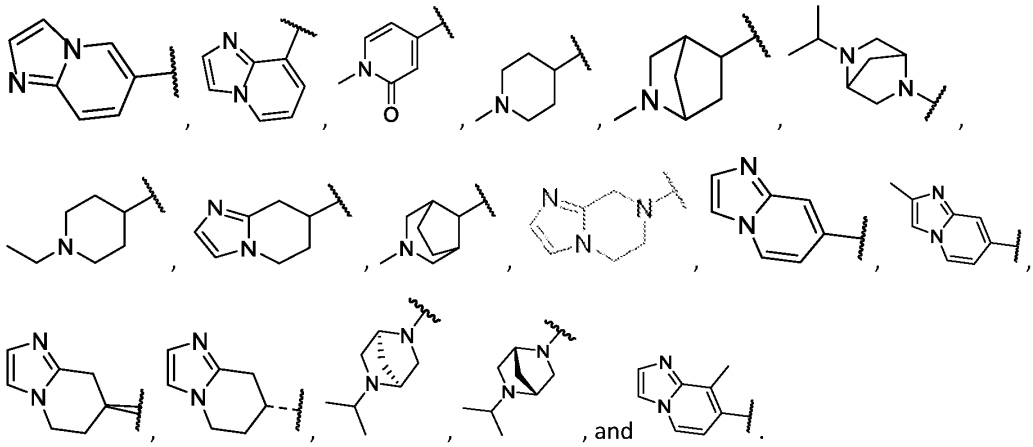




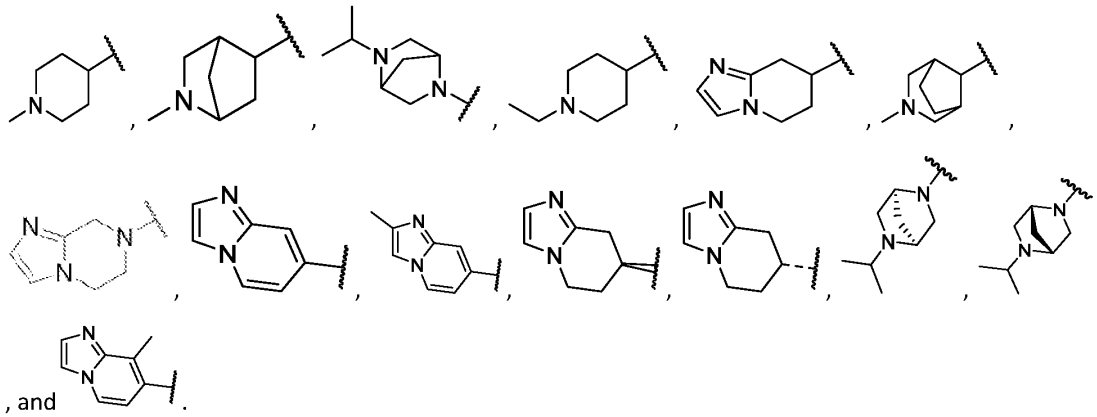
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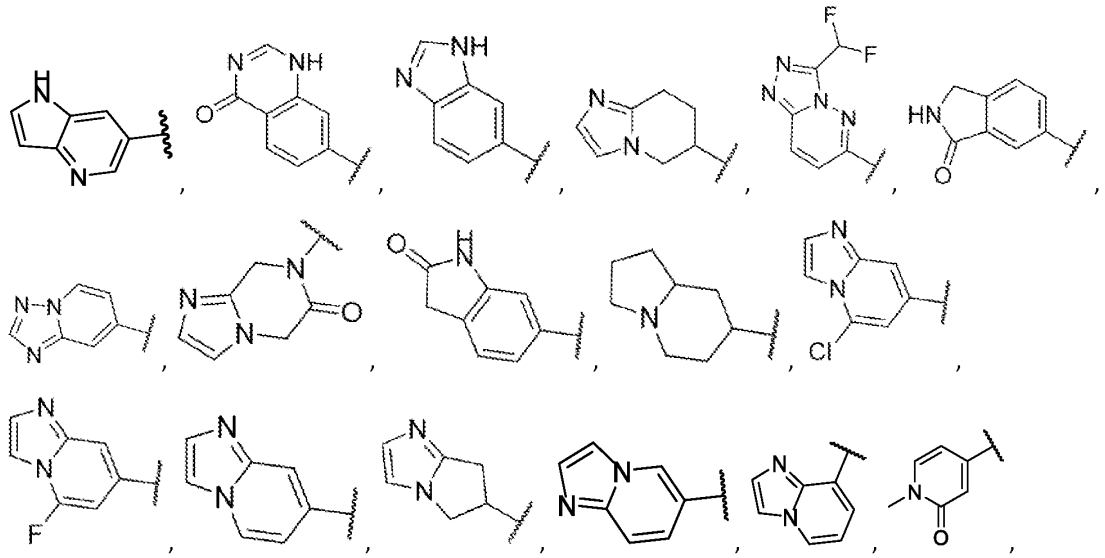
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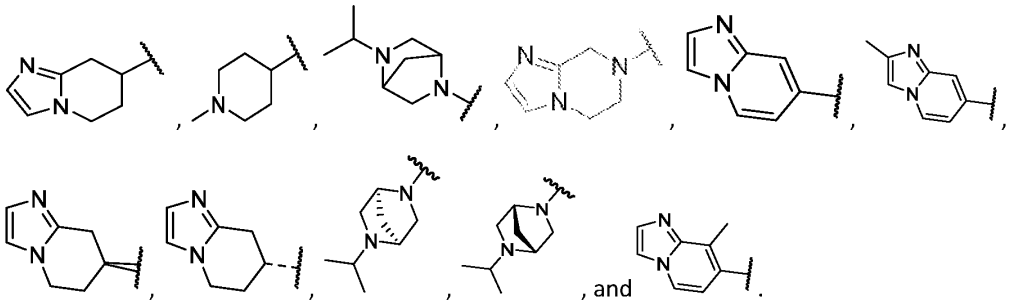


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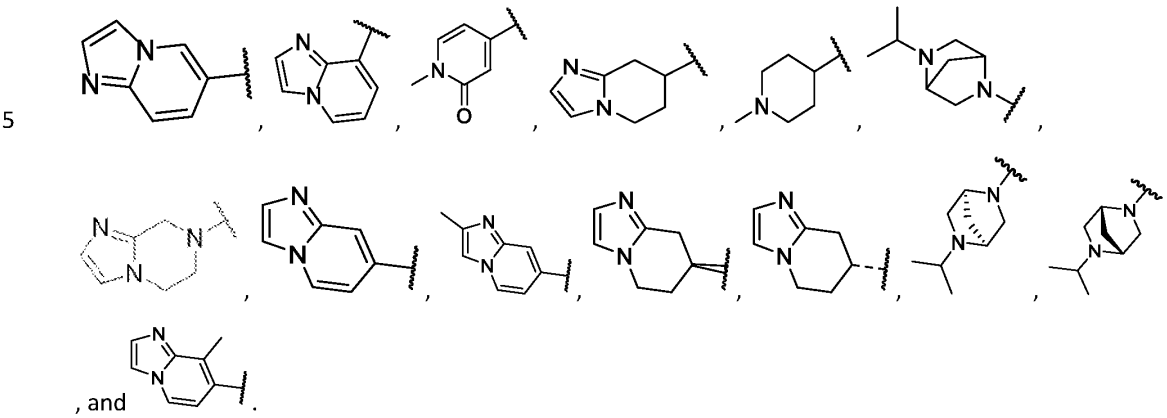


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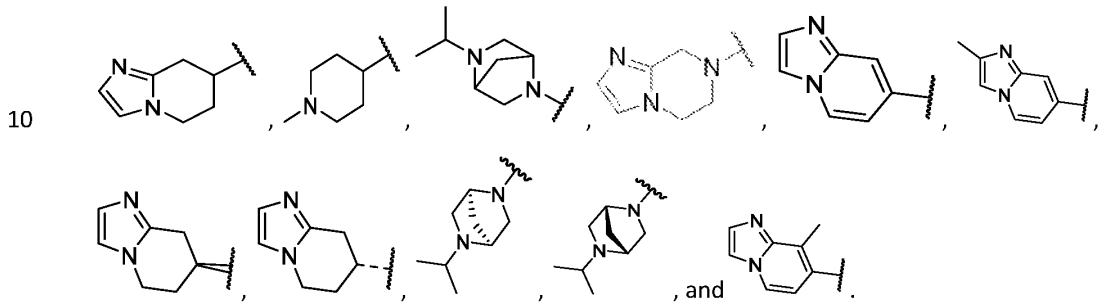




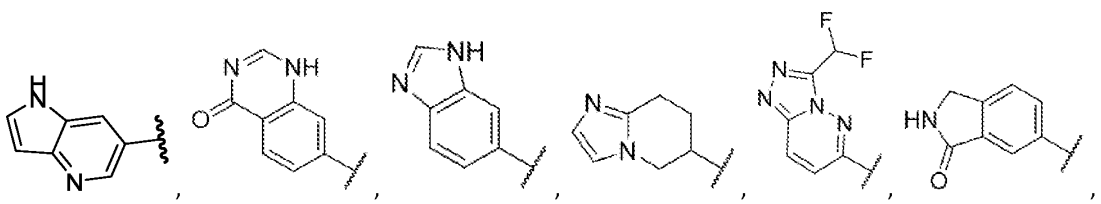
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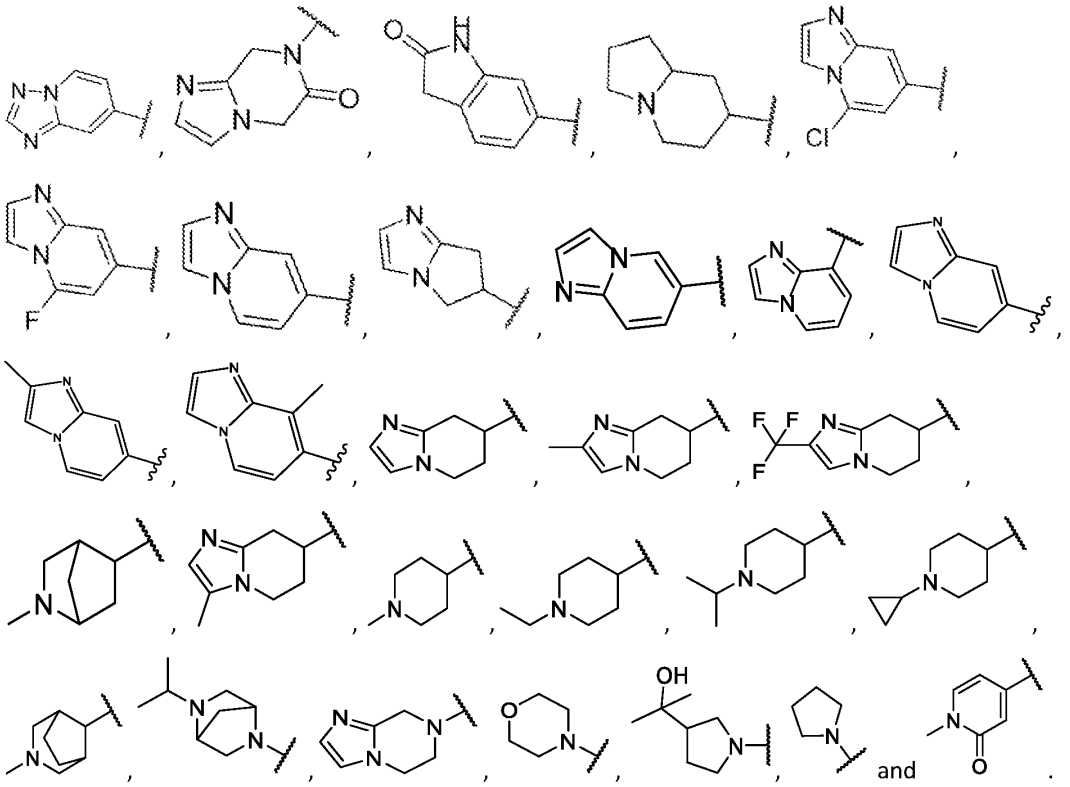


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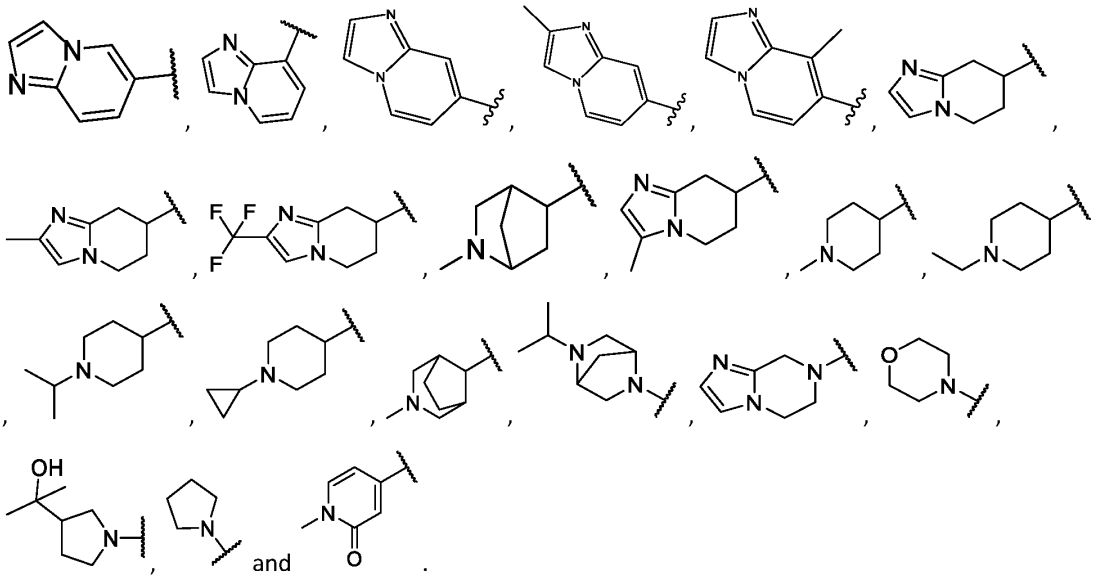


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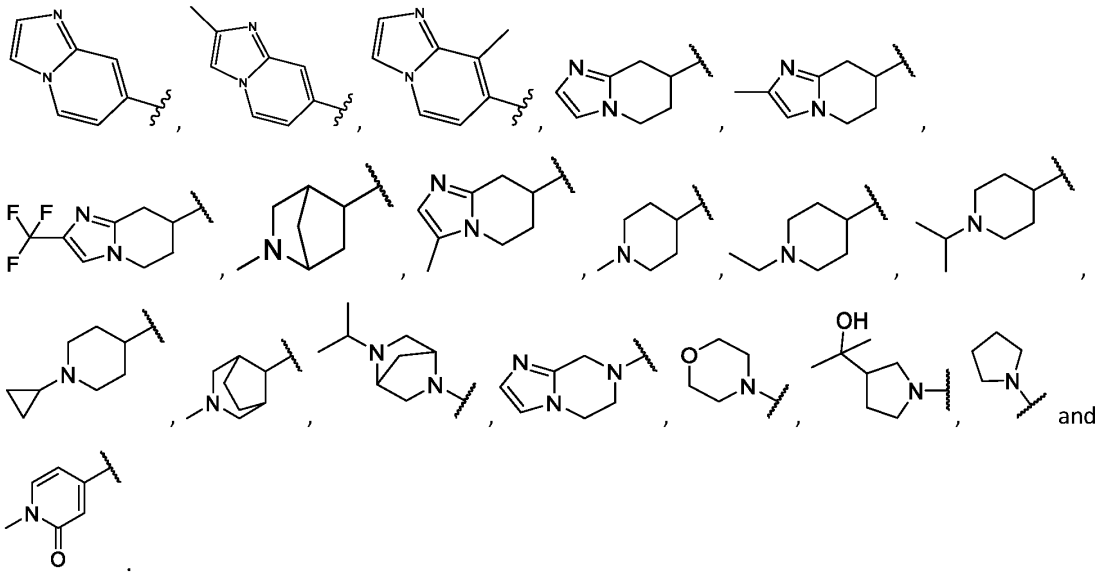




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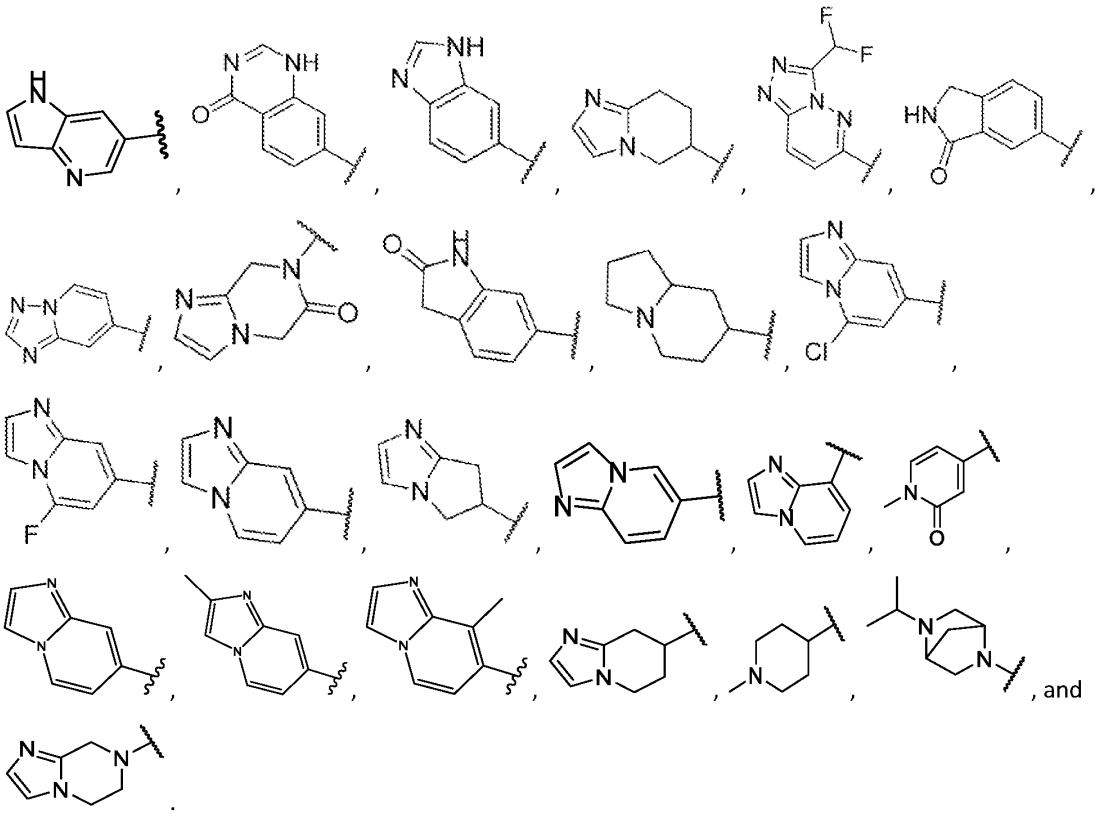
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and

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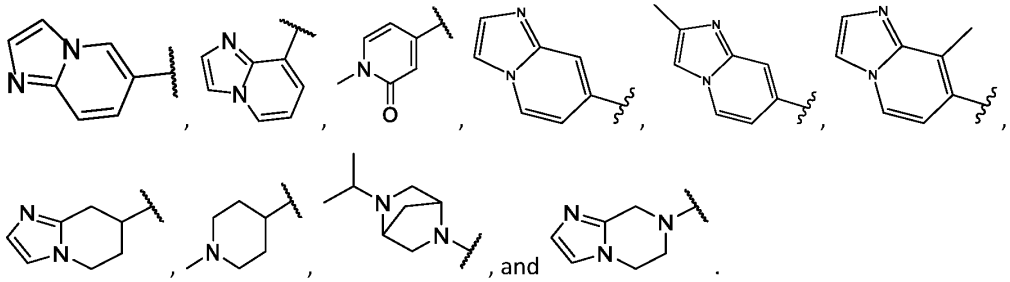
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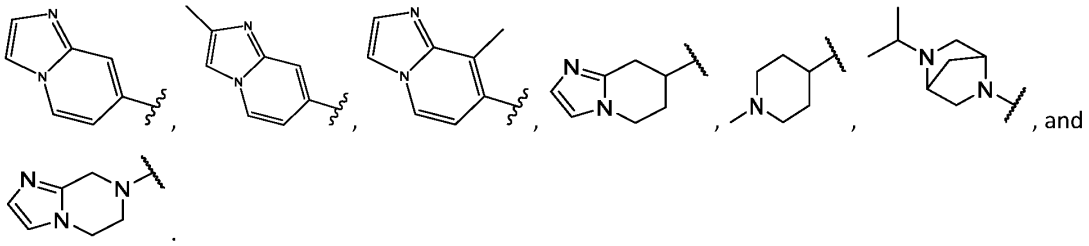
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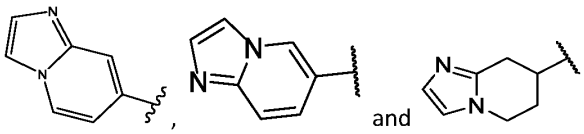
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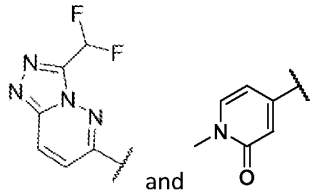


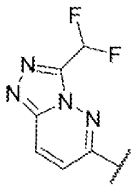
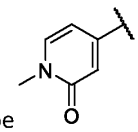
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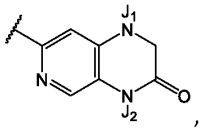
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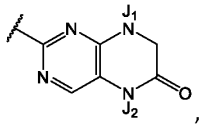


Alternatively, A is selected from: 

Specifically, A can be  .Specifically, A can be  .

Preferably, A is not:

(i)  , which may be optionally substituted at J_1, J_2, or any other ring position on A; or

(ii)  , which may be optionally substituted at J_1, J_2, or any other ring position on A.

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

$-O-(CHR12)-A$, $-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-O-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-NH-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-NR12-(CH_2)_{1-3}$ $-C(=O)-A$ and $-C(=O)NR12-(CH_2)_{0-3}-A$; and A is a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro.

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$,

$-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

$-O-(CHR12)-A$, $-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-O-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-NH-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-NR12-(CH_2)_{1-3}$ $-C(=O)-A$ and $-C(=O)NR12-(CH_2)_{0-3}-A$; and A is a 4- to 12- membered mono- or bi- cyclic ring system,

containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro.

Preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-O-(CHR12)-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$ -C(=O)-A and -C(=O)NR12-$(CH_2)_{0-3}$-A; and A is a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro.

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

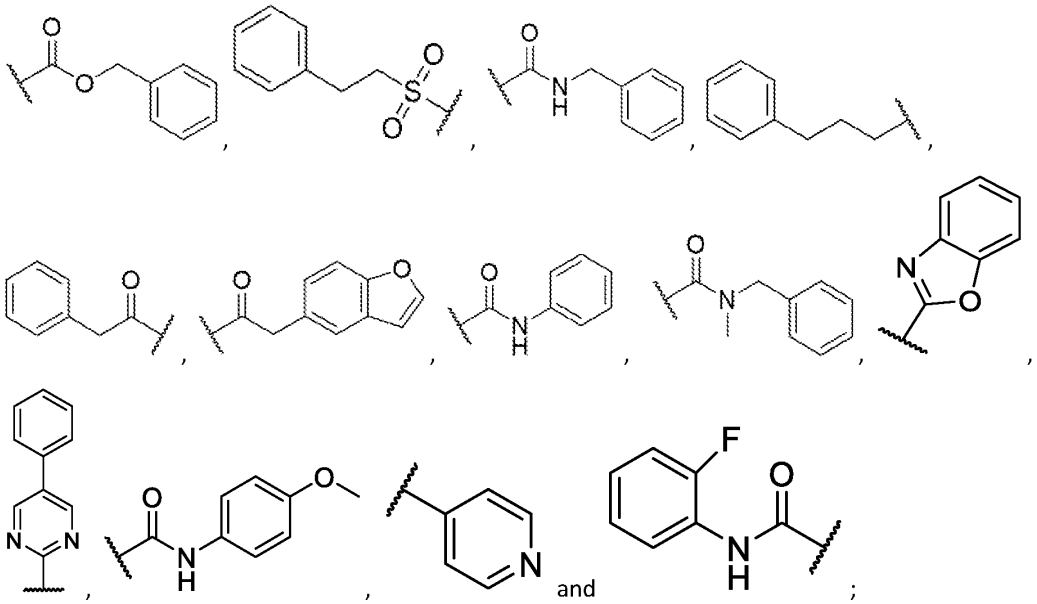
$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-O-(CHR12)-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$ -C(=O)-A and -C(=O)NR12-$(CH_2)_{0-3}$-A; and A is a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro.

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



AW- is selected from:

-O-(CHR12)-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A and -C(=O)NR12-$(CH_2)_{0-3}$-A; and A is a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro.

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-O-(CHR12)-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A and -C(=O)NR12-$(CH_2)_{0-3}$-A; and A is a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro.

Preferably, AW- is selected from:

-O-(CHR12)-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A and -C(=O)NR12-$(CH_2)_{0-3}$-A; and A is a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro.

More specifically, when not absent, -V-Z- is selected from -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 6- to 12- membered bicyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein the bicyclic ring system is fused, bridged or spiro.

More specifically, when not absent, -V-Z- is selected from-CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 6- to 12- membered bicyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein the bicyclic ring system is fused, bridged or spiro.

More specifically, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

$-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-O-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-NH-(CH_2)_{0-3}-A$ and $-(CH_2)_{0-3}-NR12-(CH_2)_{1-3}-C(=O)-A$;

and A is a 6- to 12- membered bicyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein the bicyclic ring system is fused, bridged or spiro.

More specifically, -V-Z- is selected from $-CH_2-$, $-O-CH_2-$, $-CH_2-O-$, $-CH_2-CH_2-O-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

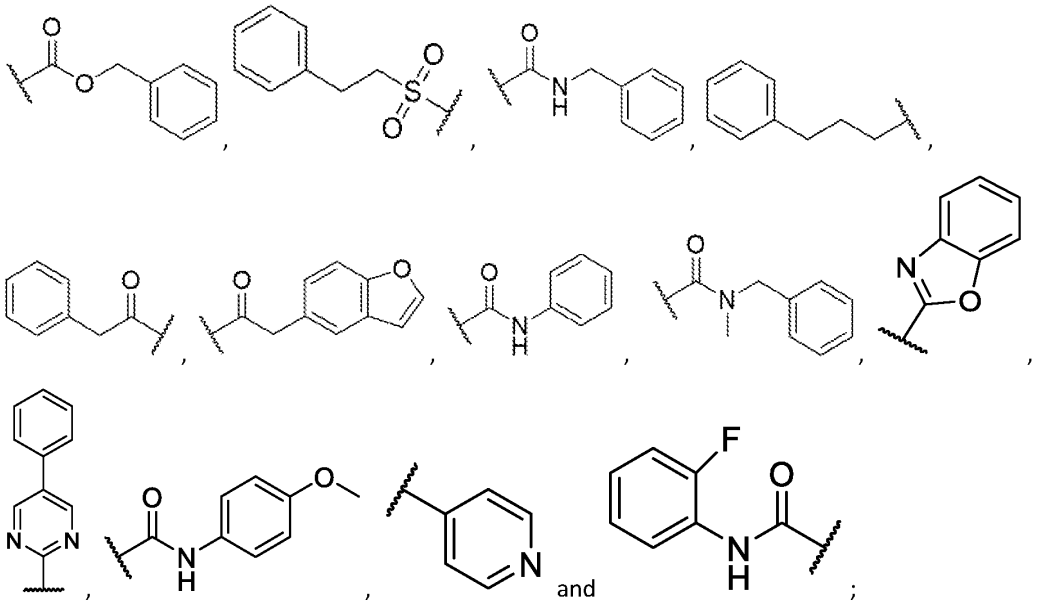
wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

$-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-O-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-NH-(CH_2)_{0-3}-A$ and $-(CH_2)_{0-3}-NR12-(CH_2)_{1-3}-C(=O)-A$;

and A is a 6- to 12- membered bicyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein the bicyclic ring system is fused, bridged or spiro.

More specifically, -V-Z- is selected from $-CH_2-$, $-O-CH_2-$, $-CH_2-O-$, $-CH_2-CH_2-O-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$, wherein R18 is selected from:



AW- is selected from:

$-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and $-(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 6- to 12- membered bicyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein the bicyclic ring system is fused, bridged or spiro.

More specifically, -V-Z- is selected from $-CH_2$-, -O-CH_2-, $-CH_2$-O- and $-CH_2-CH_2$-O-;

AW- is selected from:

$-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and $-(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 6- to 12- membered bicyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein the bicyclic ring system is fused, bridged or spiro.

More specifically, AW- is selected from:

$-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and $-(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 6- to 12- membered bicyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system

is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein the bicyclic ring system is fused, bridged or spiro.

Alternatively, when not absent, -V-Z- is selected from:

-V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one further ring member independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl.

Alternatively, when not absent, -V-Z- is selected from:

-V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one

or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one further ring member independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl.

Alternatively, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;
AW- is selected from:
-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one further ring member independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl.

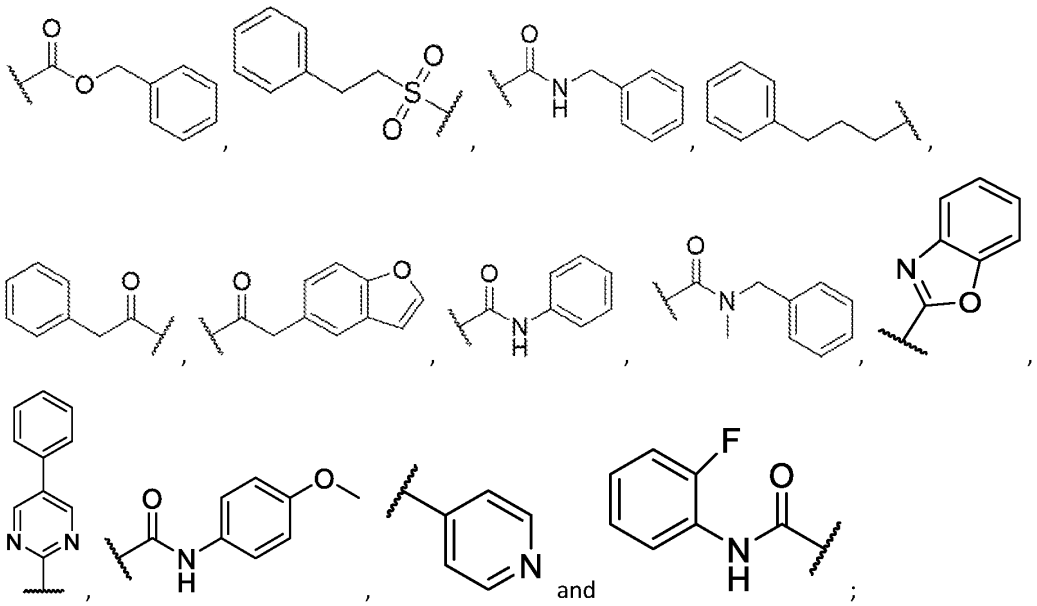
Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;
AW- is selected from:

-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one further ring member independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl.

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



AW- is selected from:

-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14,

NR13R14, CF_3, CN. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one further ring member independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl.

Alternatively, -V-Z- is selected from $-CH_2-$, $-O-CH_2-$, $-CH_2-O-$ and $-CH_2-CH_2-O-$;

AW- is selected from:

$-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}-O-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}-NH-(CH_2)_{0-3}$-A and $-(CH_2)_{0-3}-NR12-(CH_2)_{1-3}-C(=O)$-A; and A is a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one further ring member independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl.

Alternatively, AW- is selected from:

$-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}-O-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}-NH-(CH_2)_{0-3}$-A and $-(CH_2)_{0-3}-NR12-(CH_2)_{1-3}-C(=O)$-A; and A is a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one further ring member independently selected from N, optionally wherein the ring system is

substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl.

More preferably, AW- is selected from:

-(CHR12)$_{0-6}$-A (e.g. -(CHR12)$_{0-3}$-A, specifically –(CH$_2$)-A) and -(CH$_2$)$_{0-6}$-O-(CH$_2$)$_{0-6}$-A (e.g. -(CH$_2$)$_{0-3}$-O-(CH$_2$)$_{0-3}$-A, specifically –(CH$_2$)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -(CH$_2$)$_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF$_3$, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic.

More preferably, when not absent, -V-Z- is selected from: -CH$_2$-, -O-CH$_2$-, -O-C(CH$_3$)$_2$-, -CH$_2$-O-, -C(CH$_3$)$_2$-O-, -NH-CH$_2$-, -CH$_2$-NH-, -N(COCH$_3$)-CH$_2$, -CH$_2$-N(COCH$_3$), -CH$_2$-CH$_2$-, -O-CH$_2$-CH$_2$, -CH$_2$-O-CH$_2$, -CH$_2$-CH$_2$-O-, -CH$_2$-CH$_2$-CH$_2$- -CH$_2$-N(R18)- and -N(R18)-CH$_2$- wherein R18 is selected from: (CH$_2$)$_{0-6}$-aryl, (CH$_2$)$_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO$_2$R19; wherein R19 is selected from alkyl, (CH$_2$)$_{0-6}$-aryl and (CH$_2$)$_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH$_2$ or -CH$_2$CH$_2$-;

AW- is selected from:

-(CHR12)-A (specifically –(CH$_2$)-A), -(CH$_2$)$_{0-6}$-C(=O)-(CH$_2$)$_{0-6}$-A (e.g. -(CH$_2$)$_{0-3}$-C(=O)-(CH$_2$)$_{0-3}$-A , specifically –C(=O)-A) and -(CH$_2$)$_{0-6}$-O-(CH$_2$)$_{0-6}$-A (e.g. -(CH$_2$)$_{0-3}$-O-(CH$_2$)$_{0-3}$-A, specifically –(CH$_2$)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -(CH$_2$)$_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF$_3$, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic.

More preferably, when not absent, -V-Z- is selected from: -CH$_2$-, -O-CH$_2$-, -O-C(CH$_3$)$_2$-, -CH$_2$-O-, -C(CH$_3$)$_2$-O-, -NH-CH$_2$-, -CH$_2$-NH-, -N(COCH$_3$)-CH$_2$, -CH$_2$-N(COCH$_3$), -CH$_2$-CH$_2$-, -O-CH$_2$-CH$_2$, -CH$_2$-CH$_2$-O-, -CH$_2$-CH$_2$-CH$_2$- -CH$_2$-N(R18)- and -N(R18)-CH$_2$- wherein R18 is selected from: (CH$_2$)$_{0-6}$-aryl, (CH$_2$)$_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO$_2$R19; wherein R19 is selected from alkyl, (CH$_2$)$_{0-6}$-aryl and (CH$_2$)$_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH$_2$ or -CH$_2$CH$_2$-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic.

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic.

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

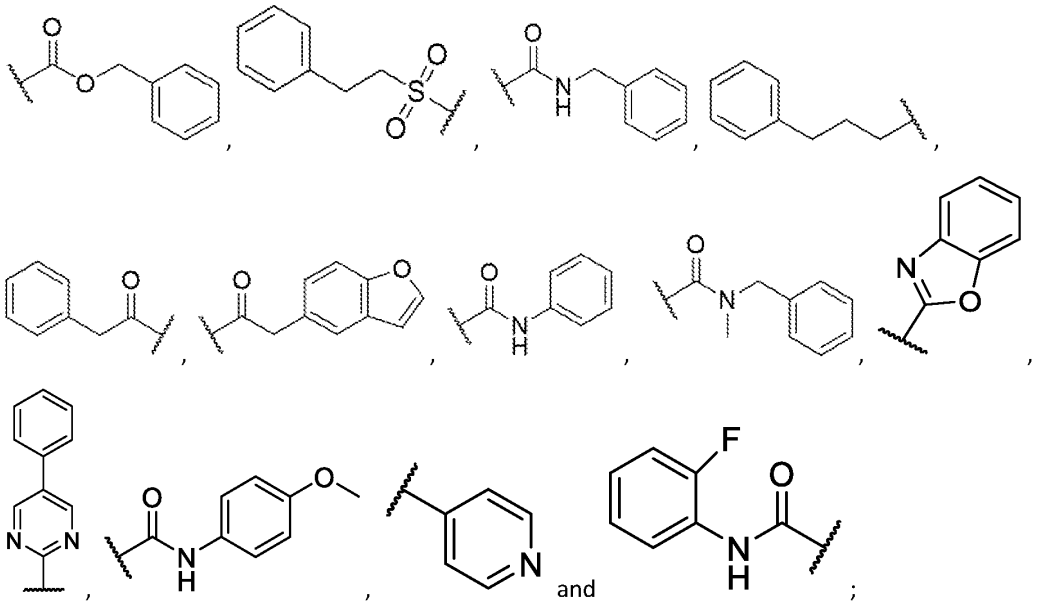
wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13,

C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic.

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic.

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the

ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic.

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic.

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13,

C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic.

More preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

-(CHR12)-A (specifically $-(CH_2)-A$), $-(CH_2)_{0-6}-C(=O)-(CH_2)_{0-6}-A$ (e.g. $-(CH_2)_{0-3}-C(=O)-(CH_2)_{0-3}-A$, specifically $-C(=O)-A$) and $-(CH_2)_{0-6}-O-(CH_2)_{0-6}-A$ (e.g. $-(CH_2)_{0-3}-O-(CH_2)_{0-3}-A$, specifically $-(CH_2)-O-A$); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic.

More preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

-(CHR12)-A (specifically $-(CH_2)-A$) and $-(CH_2)_{0-6}-O-(CH_2)_{0-6}-A$ (e.g. $-(CH_2)_{0-3}-O-(CH_2)_{0-3}-A$, specifically $-(CH_2)-O-A$); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic.

More preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic.

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic.

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

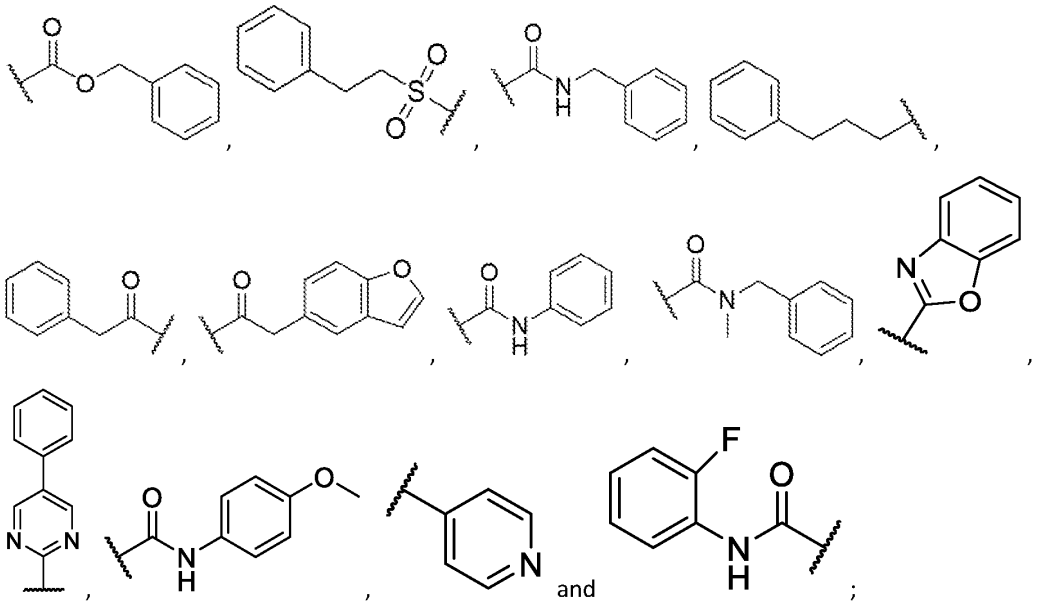
wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12,

C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic.

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic.

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12,

C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic.

More preferably, AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic.

Preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN.

Preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-

membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN.

Preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN.

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN.

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

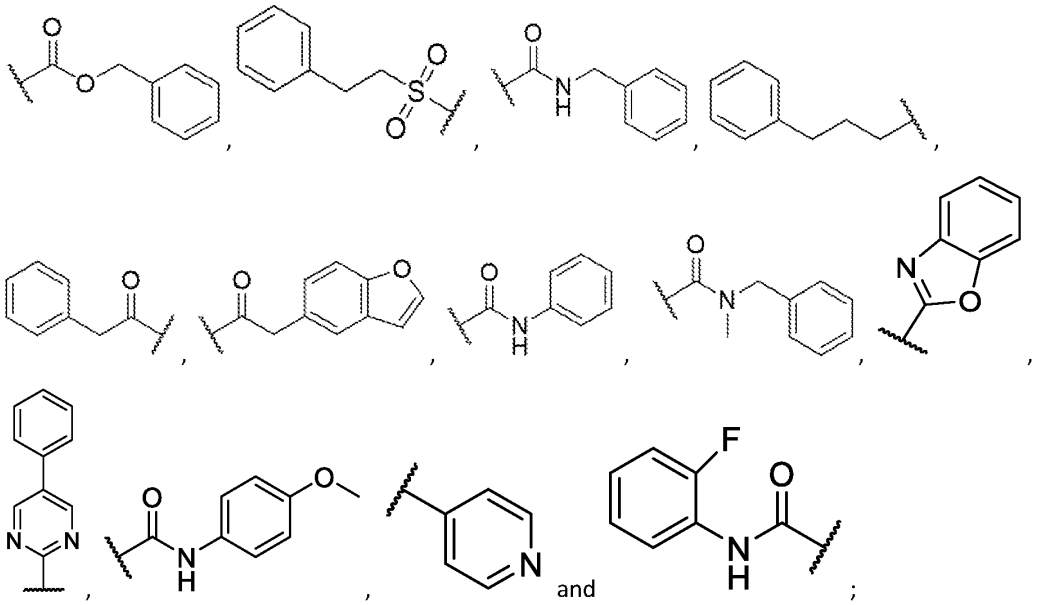
wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH,

oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN.

Preferably, -V-Z- is selected from from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN.

Preferably, AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN.

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

-(CHR12)-A (specifically $-(CH_2)$-A) and $-(CH_2)_{0-6}-O-(CH_2)_{0-6}$-A (e.g. $-(CH_2)_{0-3}-O-(CH_2)_{0-3}$-A, specifically $-(CH_2)$-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN.

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

-(CHR12)-A (specifically $-(CH_2)$-A) and $-(CH_2)_{0-6}-O-(CH_2)_{0-6}$-A (e.g. $-(CH_2)_{0-3}-O-(CH_2)_{0-3}$-A, specifically $-(CH_2)$-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN.

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

-(CHR12)-A (specifically $-(CH_2)$-A) and $-(CH_2)_{0-6}-O-(CH_2)_{0-6}$-A (e.g. $-(CH_2)_{0-3}-O-(CH_2)_{0-3}$-A, specifically $-(CH_2)$-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN.

Preferably, -V-Z- is selected from from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

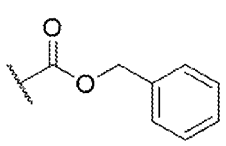
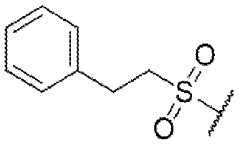
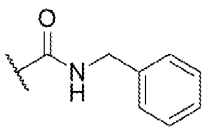
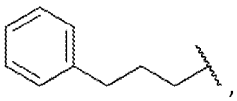
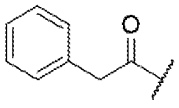
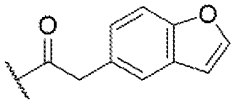
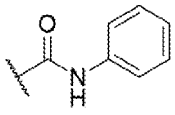
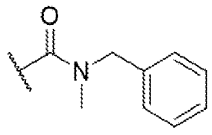
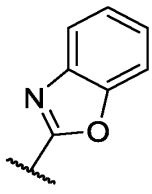
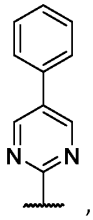
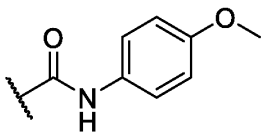
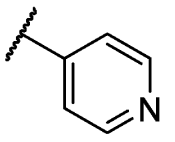
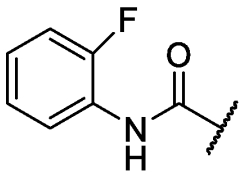
$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN.

Preferably, -V-Z- is selected from from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:


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and

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AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN.

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN.

Preferably, AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN.

Preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-O-(CHR12)-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$ -C(=O)-A and -C(=O)NR12-$(CH_2)_{0-3}$-A; and A is a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro; and X is CH_2 and Y is NH or N.

Preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-O-(CHR12)-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A and -C(=O)NR12-$(CH_2)_{0-3}$-A; and A is a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro; and X is CH_2 and Y is NH or N.

Preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-O-(CHR12)-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A and -C(=O)NR12-$(CH_2)_{0-3}$-A; and A is a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro; and X is CH_2 and Y is NH or N.

Preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-O-(CHR12)-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A and -C(=O)NR12-$(CH_2)_{0-3}$-A; and A is a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro; and X is CH_2 and Y is NH.

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

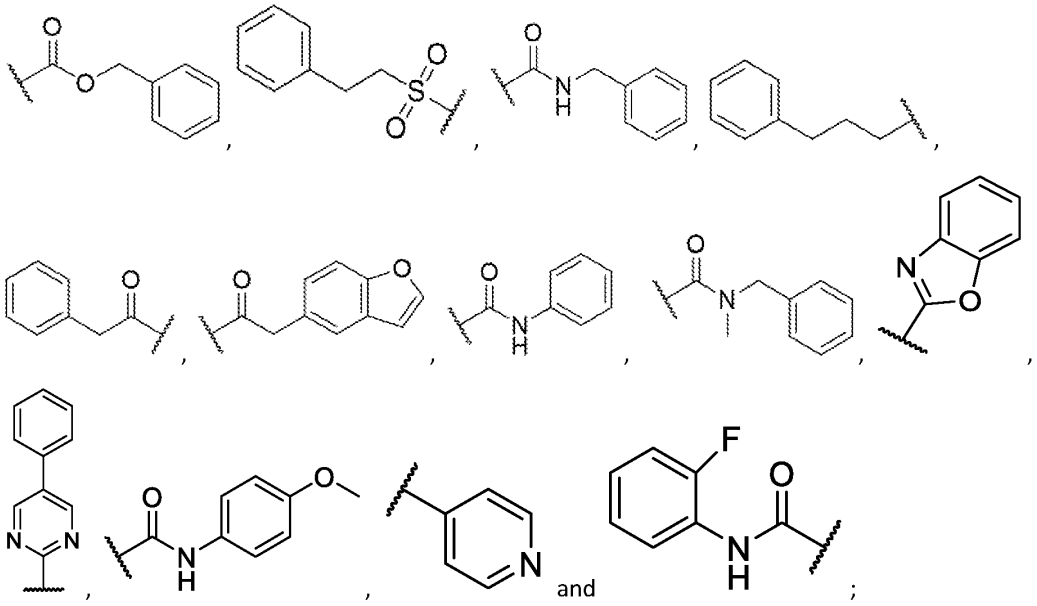
$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-O-(CHR12)-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$ -C(=O)-A and -C(=O)NR12-$(CH_2)_{0-3}$-A; and A is a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro; and X is CH_2 and Y is NH.

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



AW- is selected from:

-O-(CHR12)-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$ -C(=O)-A and -C(=O)NR12-$(CH_2)_{0-3}$-A; and A is a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl,

heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro; and X is CH_2 and Y is NH.

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-O-(CHR12)-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$ -C(=O)-A and -C(=O)NR12-$(CH_2)_{0-3}$-A; and A is a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro; and X is CH_2 and Y is NH.

Preferably, AW- is selected from:

-O-(CHR12)-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$ -C(=O)-A and -C(=O)NR12-$(CH_2)_{0-3}$-A; and A is a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro; and X is CH_2 and Y is NH.

More specifically, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 6- to 12- membered bicyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14,

NR13R14, CF_3, CN; wherein the bicyclic ring system is fused, bridged or spiro; and X is CH_2 and Y is NH or N.

More specifically, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

$-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}-O-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}-NH-(CH_2)_{0-3}$-A and $-(CH_2)_{0-3}-NR12-(CH_2)_{1-3}-C(=O)$-A; and A is a 6- to 12- membered bicyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein the bicyclic ring system is fused, bridged or spiro; and X is CH_2 and Y is NH or N.

More specifically, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

$-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}-O-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}-NH-(CH_2)_{0-3}$-A and $-(CH_2)_{0-3}-NR12-(CH_2)_{1-3}-C(=O)$-A; and A is a 6- to 12- membered bicyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein the bicyclic ring system is fused, bridged or spiro; and X is CH_2 and Y is NH or N.

More specifically, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 6- to 12- membered bicyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein the bicyclic ring system is fused, bridged or spiro; and X is CH_2 and Y is NH.

More specifically, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

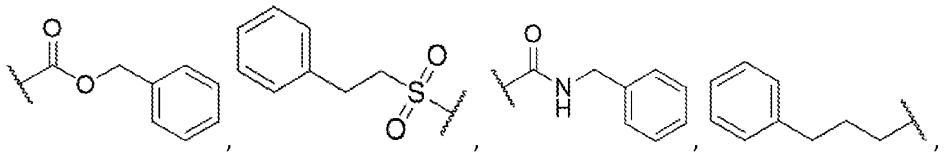
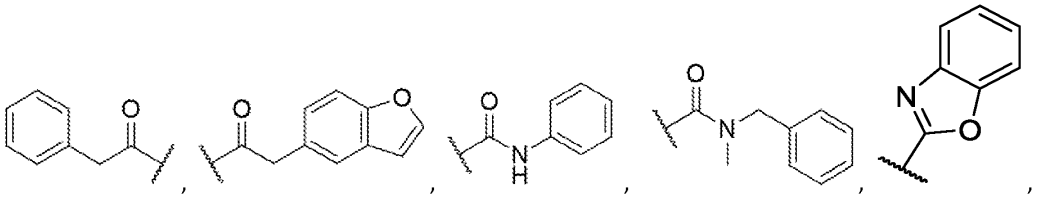
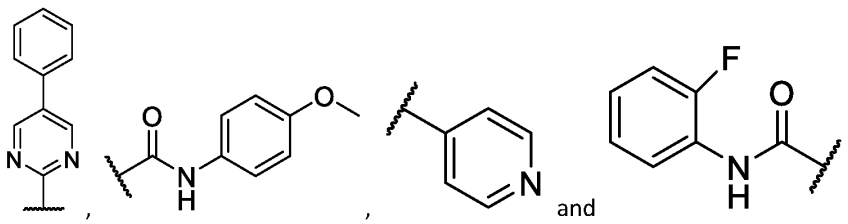
$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 6- to 12- membered bicyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein the bicyclic ring system is fused, bridged or spiro; and X is CH_2 and Y is NH.

More specifically, -V-Z- is selected from - CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:




and ;

AW- is selected from:

$-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and $-(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 6- to 12- membered bicyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein the bicyclic ring system is fused, bridged or spiro; and X is CH_2 and Y is NH.

More specifically, -V-Z- is selected from $-CH_2-$, $-O-CH_2-$, $-CH_2-O-$ and $-CH_2-CH_2-O-$;

AW- is selected from:

$-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and $-(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 6- to 12- membered bicyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein the bicyclic ring system is fused, bridged or spiro; and X is CH_2 and Y is NH.

More specifically, AW- is selected from:

$-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and $-(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 6- to 12- membered bicyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein the bicyclic ring system is fused, bridged or spiro; and X is CH_2 and Y is NH.

Alternatively, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

$-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and $-(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is

substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one further ring member independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl; and X is CH_2 and Y is NH or N.

Alternatively, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A;

and A is a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one further ring member independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl; and X is CH_2 and Y is NH or N.

Alternatively, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

$-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and $-(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one further ring member independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl; and X is CH_2 and Y is NH or N.

Alternatively, when not absent, -V-Z- is selected from: $-CH_2$-, -O-CH_2-, -O-$C(CH_3)_2$-, $-CH_2$-O-, $-C(CH_3)_2$-O-, -NH-CH_2-, $-CH_2$-NH-, -N($COCH_3$)-CH_2, $-CH_2$-N($COCH_3$), $-CH_2-CH_2$-, -O-CH_2-CH_2, $-CH_2$-O-CH_2, $-CH_2-CH_2$-O-, and $-CH_2-CH_2-CH_2$-; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2$-;

AW- is selected from:

$-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and $-(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one further ring member independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl; and X is CH_2 and Y is NH.

Alternatively, -V-Z- is selected from $-CH_2$-, -O-CH_2-, $-CH_2$-O-, $-CH_2-CH_2$-O-, $-CH_2$-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one further ring member independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl; and X is CH_2 and Y is NH.

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

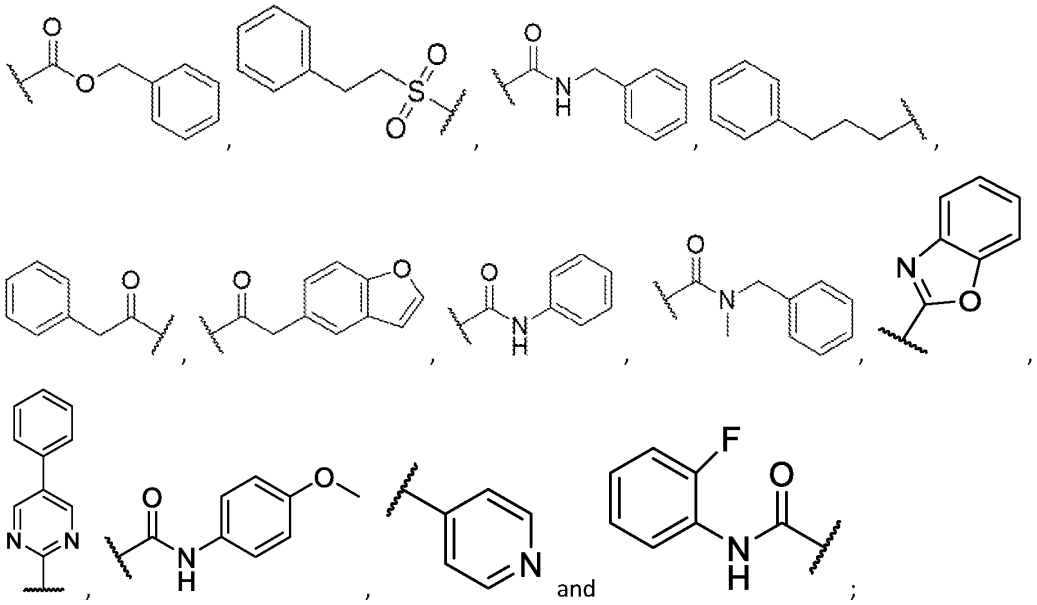
$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one further ring member independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl; and X is CH_2 and Y is NH.

Alternatively, -V-Z- is selected -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



AW- is selected from:

$-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and $-(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one further ring member independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl; and X is CH_2 and Y is NH.

Alternatively, -V-Z- is selected from $-CH_2$-, -O-CH_2-, $-CH_2$-O- and $-CH_2$-CH_2-O-;

AW- is selected from:

$-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and $-(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14,

NR13R14, CF_3, CN. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one further ring member independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl; and X is CH_2 and Y is NH.

Alternatively, AW- is selected from:

$-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and $-(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one further ring member independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl; and X is CH_2 and Y is NH.

More preferably, AW- is selected from:

$-(CHR12)_{0-6}$-A (e.g. $-(CHR12)_{0-3}$-A, specifically $-(CH_2)$-A) and $-(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. $-(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically $-(CH_2)$-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is NH.

More preferably, when not absent, -V-Z- is selected from: $-CH_2$-, -O-CH_2-, -O-$C(CH_3)_2$-, $-CH_2$-O-, $-C(CH_3)_2$-O-, -NH-CH_2-, $-CH_2$-NH-, -N($COCH_3$)-CH_2, $-CH_2$-N($COCH_3$), $-CH_2$-CH_2-, -O-CH_2-CH_2, $-CH_2$-O-CH_2, $-CH_2$-CH_2-O-, $-CH_2$-CH_2-CH_2- $-CH_2$-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is NH or N.

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is NH or N.

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or

10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is NH or N.

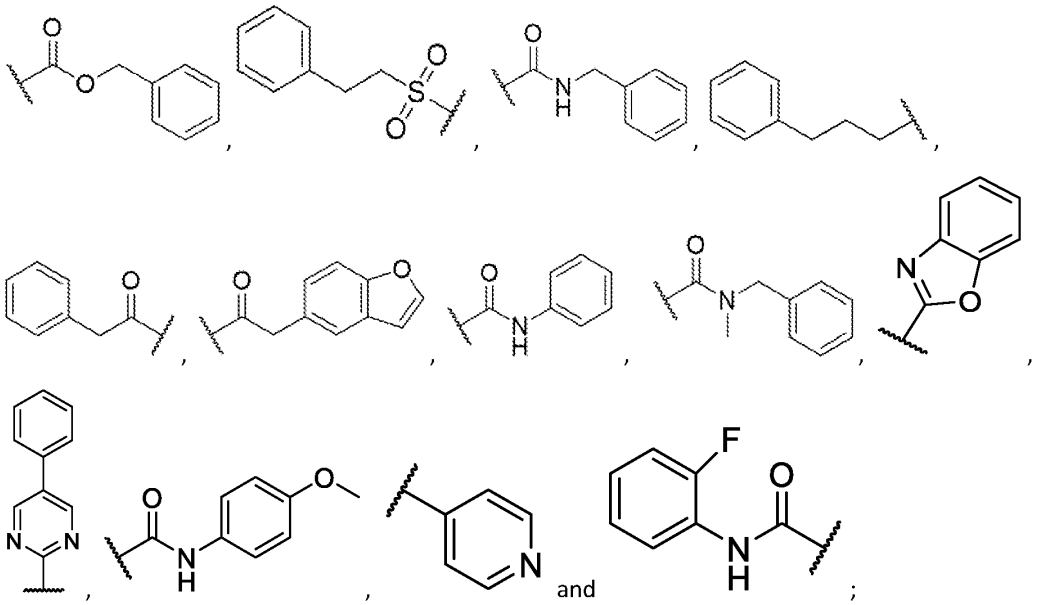
More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;
AW- is selected from:
-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is NH.

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;
AW- is selected from:
-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is NH.

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is NH.

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13,

C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is NH.

More preferably, AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is NH.

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is NH or N.

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is NH or N.

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;
AW- is selected from:
-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is NH or N.

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;
AW- is selected from:
-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is NH.

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

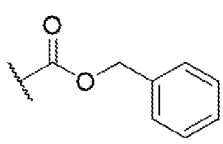
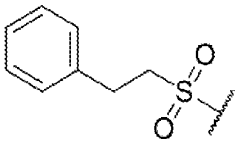
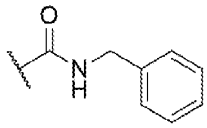
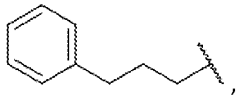
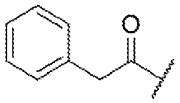
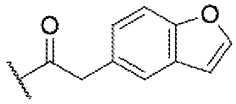
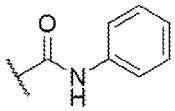
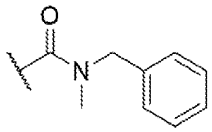
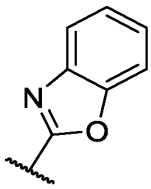
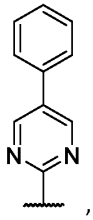
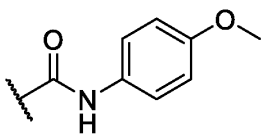
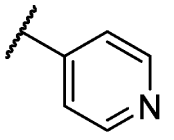
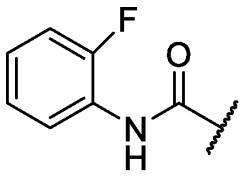
$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is NH.

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:


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and

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AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is NH.

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is NH.

More preferably, AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is NH.

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is O.

More preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

AW- is selected from:

-(CHR12)-A (specifically $-(CH_2)$-A), $-(CH_2)_{0-6}-C(=O)-(CH_2)_{0-6}$-A (e.g. $-(CH_2)_{0-3}-C(=O)-(CH_2)_{0-3}$-A , specifically –C(=O)-A) and $-(CH_2)_{0-6}-O-(CH_2)_{0-6}$-A (e.g. $-(CH_2)_{0-3}-O-(CH_2)_{0-3}$-A, specifically $-(CH_2)-O$-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is O.

More preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

-(CHR12)-A (specifically $-(CH_2)$-A), $-(CH_2)_{0-6}-C(=O)-(CH_2)_{0-6}$-A (e.g. $-(CH_2)_{0-3}-C(=O)-(CH_2)_{0-3}$-A , specifically –C(=O)-A) and $-(CH_2)_{0-6}-O-(CH_2)_{0-6}$-A (e.g. $-(CH_2)_{0-3}-O-(CH_2)_{0-3}$-A, specifically $-(CH_2)-O$-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is O.

More preferably, -V-Z- is selected from $-CH_2-$, $-O-CH_2-$, $-CH_2-O-$, $-CH_2-CH_2-O-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$, wherein R18 is selected from:

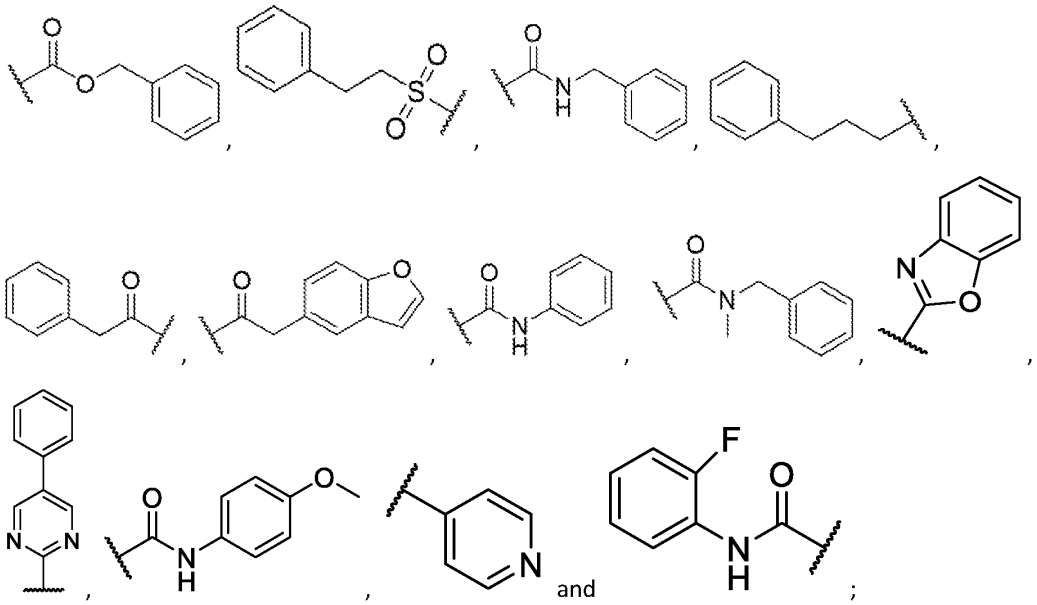
$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is O.

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is O.

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is O.

More preferably, AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is O.

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is O.

More preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

AW- is selected from:

-(CHR12)-A (specifically $-(CH_2)$-A) and $-(CH_2)_{0-6}-O-(CH_2)_{0-6}$-A (e.g. $-(CH_2)_{0-3}-O-(CH_2)_{0-3}$-A, specifically $-(CH_2)$-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is O.

More preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

-(CHR12)-A (specifically $-(CH_2)$-A) and $-(CH_2)_{0-6}-O-(CH_2)_{0-6}$-A (e.g. $-(CH_2)_{0-3}-O-(CH_2)_{0-3}$-A, specifically $-(CH_2)$-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is O.

More preferably, -V-Z- is selected from $-CH_2-$, $-O-CH_2-$, $-CH_2-O-$, $-CH_2-CH_2-O-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

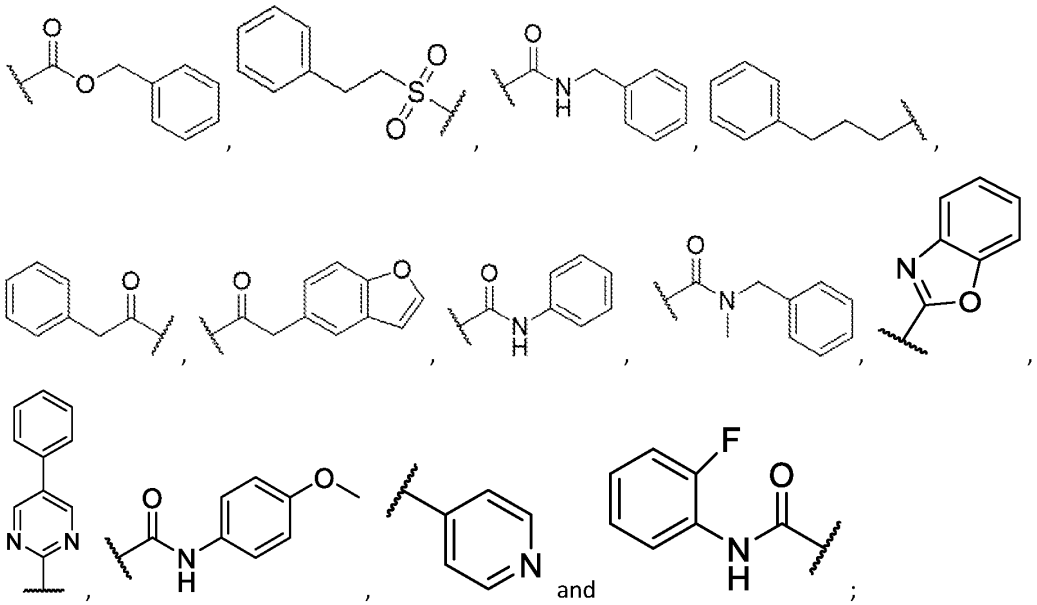
wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-(CHR12)-A (specifically $-(CH_2)$-A) and $-(CH_2)_{0-6}-O-(CH_2)_{0-6}$-A (e.g. $-(CH_2)_{0-3}-O-(CH_2)_{0-3}$-A, specifically $-(CH_2)$-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring

member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is O.

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is O.

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring

member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is O.

More preferably, AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; and X is CH_2 and Y is O.

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH or N.

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH or N.

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH or N.

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH.

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

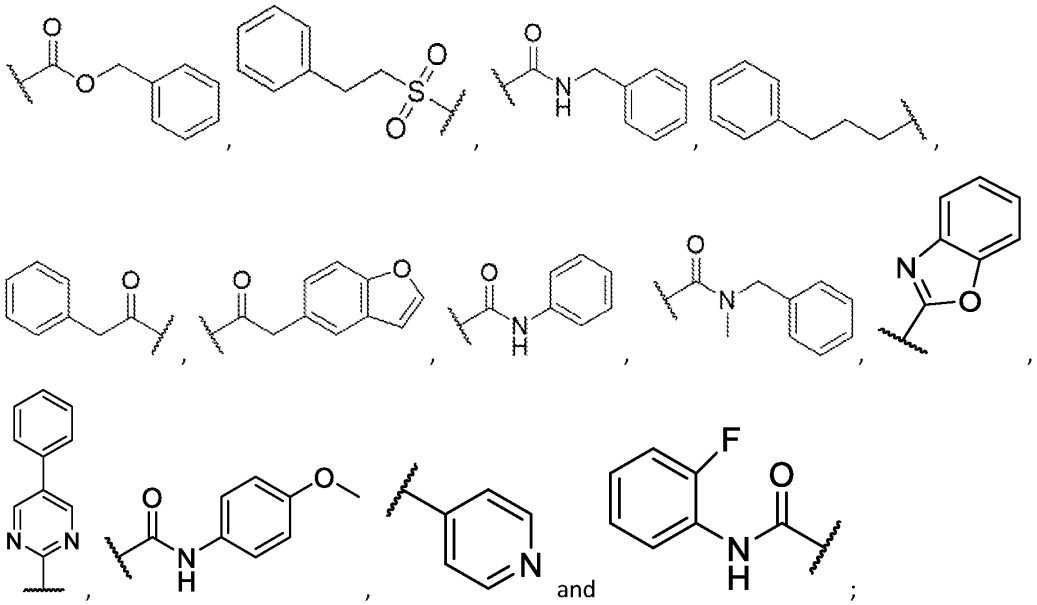
$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH.

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH.

More preferably, AW- is selected from:
-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH.

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;
AW- is selected from:
-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH or N.

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;
AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH or N.

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;
AW- is selected from:
-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH or N.

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;
AW- is selected from:
-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH.

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

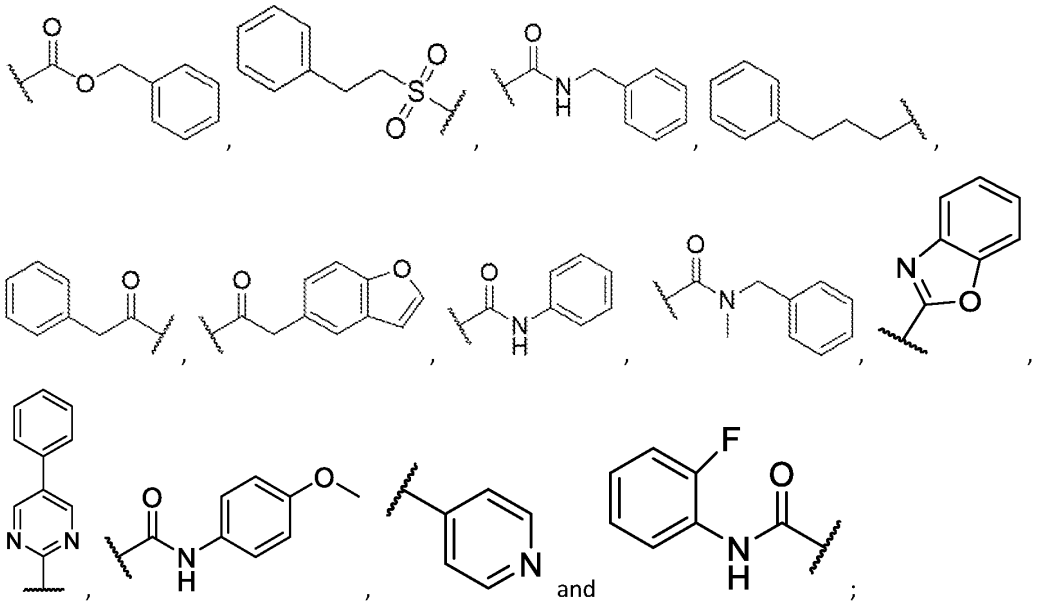
$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:
-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from

halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH.

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH.

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH.

More preferably, AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH.

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is O.

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is O.

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is O.

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

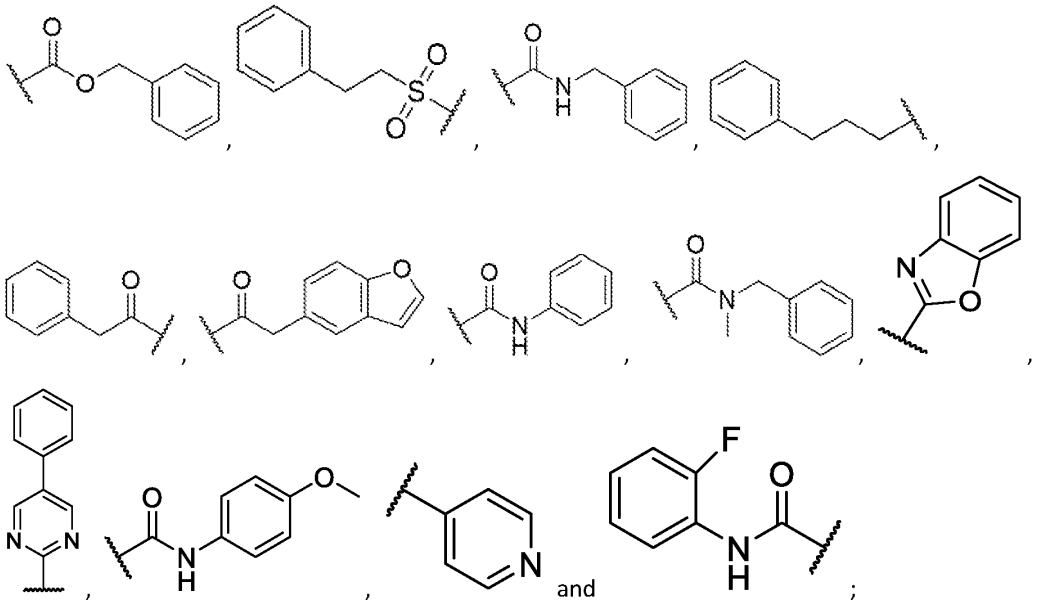
$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is O.

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is O.

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is O.

More preferably, AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is

substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is O.

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];
AW- is selected from:
-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is O.

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];
AW- is selected from:
-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is O.

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;
AW- is selected from:
-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from

halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is O.

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

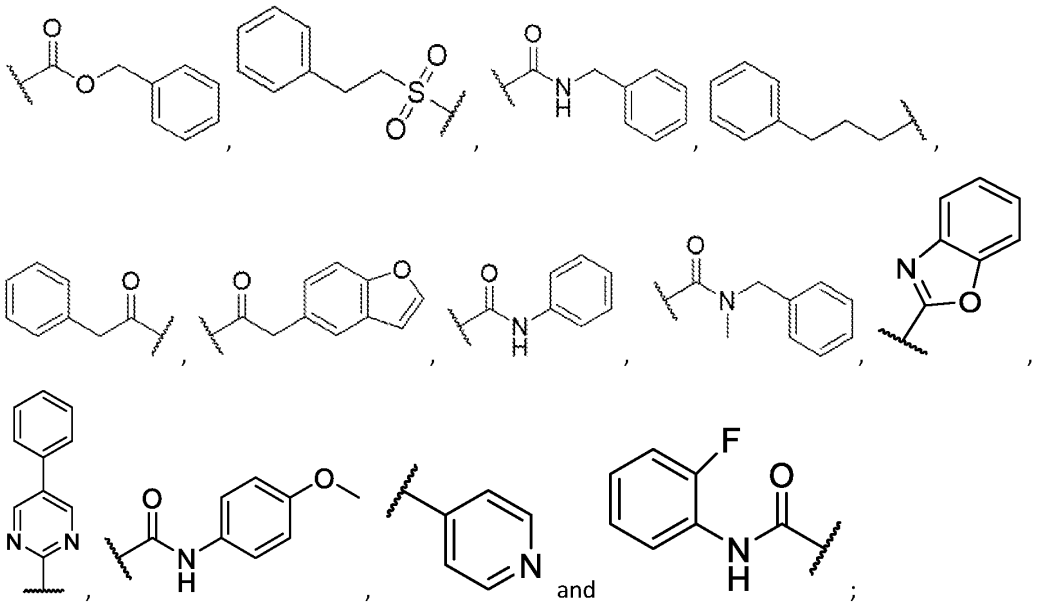
$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is O.

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



and ;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from

halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is O.

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is O.

More preferably, AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is O.

-CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-,

-$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-O-(CHR12)-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$ -C(=O)-A and -C(=O)NR12-$(CH_2)_{0-3}$-A; and A is a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro; X is CH_2 and Y is NH or N; and B is heteroaryl[a].

Preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-,

$-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

$-O-(CHR12)-A$, $-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-O-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-NH-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-NR12-(CH_2)_{1-3}$ $-C(=O)-A$ and $-C(=O)NR12-(CH_2)_{0-3}-A$; and A is a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro; X is CH_2 and Y is NH or N; and B is heteroaryl[a].

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

$-O-(CHR12)-A$, $-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-O-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-NH-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-NR12-(CH_2)_{1-3}$ $-C(=O)-A$ and $-C(=O)NR12-(CH_2)_{0-3}-A$; and A is a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro; X is CH_2 and Y is NH or N; and B is heteroaryl[a].

Preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

$-O-(CHR12)-A$, $-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-O-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-NH-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-NR12-(CH_2)_{1-3}$ $-C(=O)-A$ and $-C(=O)NR12-(CH_2)_{0-3}-A$; and A is a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently

selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro; X is CH_2 and Y is NH; and B is heteroaryl[a].

Preferably, -V-Z- is selected from CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

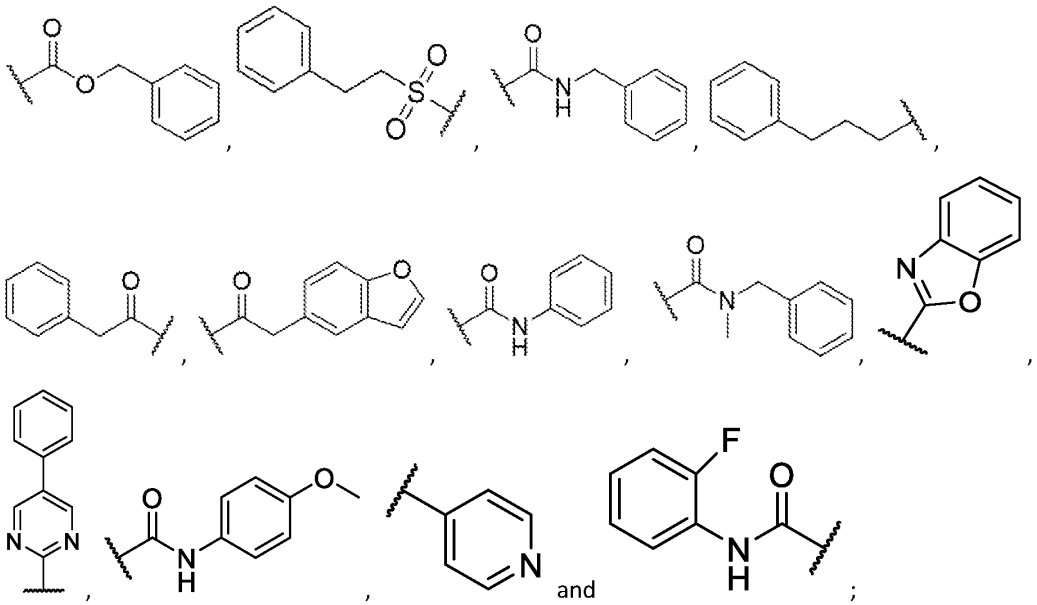
$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-O-(CHR12)-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$ -C(=O)-A and -C(=O)NR12-$(CH_2)_{0-3}$-A; and A is a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro; X is CH_2 and Y is NH; and B is heteroaryl[a].

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



AW- is selected from:

-O-(CHR12)-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$ -C(=O)-A and -C(=O)NR12-$(CH_2)_{0-3}$-A; and A is a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro; X is CH_2 and Y is NH; and B is heteroaryl[a].

Preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-O-(CHR12)-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$ -C(=O)-A and -C(=O)NR12-$(CH_2)_{0-3}$-A; and A is a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro; X is CH_2 and Y is NH; and B is heteroaryl[a].

Preferably, AW- is selected from:

-O-(CHR12)-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$ -C(=O)-A and -C(=O)NR12-$(CH_2)_{0-3}$-A; and A is a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro; X is CH_2 and Y is NH; and B is heteroaryl[a].

More specifically, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

$-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and $-(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 6- to 12- membered bicyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein the bicyclic ring system is fused, bridged or spiro; X is CH_2 and Y is NH or N; and B is heteroaryl[a] and selected from isoquinolinyl and azaindole (specifically 7-azaindole), optionally substituted as for heteroaryl[a].

More specifically, when not absent, -V-Z- is selected from: $-CH_2$-, -O-CH_2-, -O-$C(CH_3)_2$-, $-CH_2$-O-, $-C(CH_3)_2$-O-, -NH-CH_2-, $-CH_2$-NH-, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2$-, -O-CH_2-CH_2, $-CH_2-CH_2$-O-, $-CH_2-CH_2-CH_2$- $-CH_2$-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2$-;

AW- is selected from:

$-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and $-(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 6- to 12- membered bicyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein the bicyclic ring system is fused, bridged or spiro; X is CH_2 and Y is NH or N; and B is heteroaryl[a] and selected from isoquinolinyl and azaindole (specifically 7-azaindole), optionally substituted as for heteroaryl[a].

More specifically, when not absent, -V-Z- is selected from: $-CH_2$-, -O-CH_2-, -O-$C(CH_3)_2$-, $-CH_2$-O-, $-C(CH_3)_2$-O-, -NH-CH_2-, $-CH_2$-NH-, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2$-, -O-CH_2-CH_2, $-CH_2$-O-CH_2, $-CH_2-CH_2$-O-, and $-CH_2-CH_2-CH_2$-; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2$-;

AW- is selected from:

$-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and $-(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 6- to 12- membered bicyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein the bicyclic ring system is fused, bridged or spiro; X is CH_2 and Y is NH or N;

and B is heteroaryl[a] and selected from isoquinolinyl and azaindole (specifically 7-azaindole), optionally substituted as for heteroaryl[a].

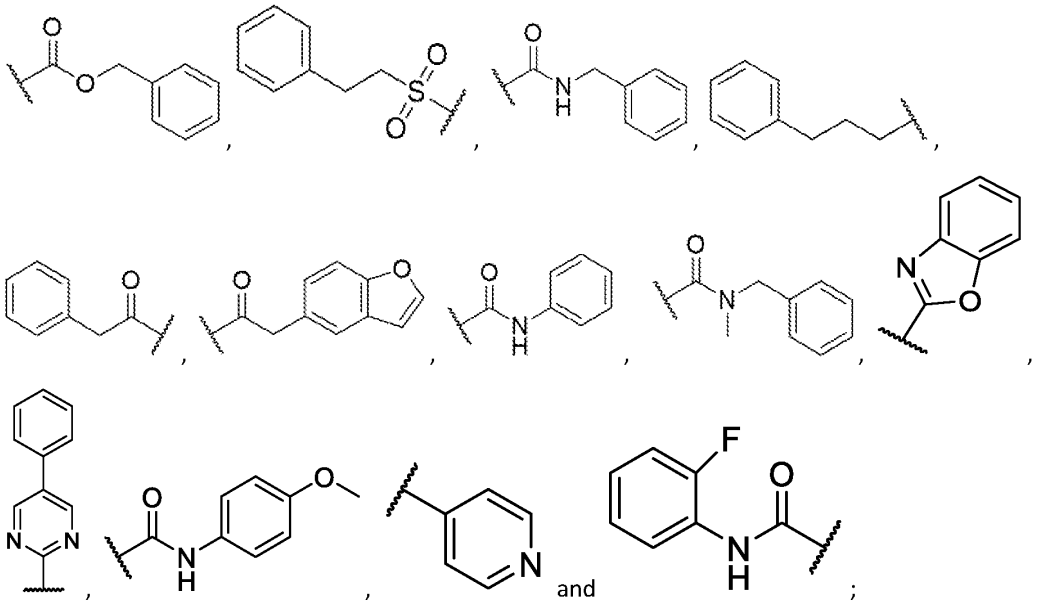
More specifically, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;
AW- is selected from:
$-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-O-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-NH-(CH_2)_{0-3}-A$ and $-(CH_2)_{0-3}-NR12-(CH_2)_{1-3}-C(=O)-A$;
and A is a 6- to 12- membered bicyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein the bicyclic ring system is fused, bridged or spiro; X is CH_2 and Y is NH; and B is heteroaryl[a] and selected from isoquinolinyl and azaindole (specifically 7-azaindole), optionally substituted as for heteroaryl[a].

More specifically, -V-Z- is selected from $-CH_2-$, $-O-CH_2-$, $-CH_2-O-$, $-CH_2-CH_2-O-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;
AW- is selected from:
$-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-O-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-NH-(CH_2)_{0-3}-A$ and $-(CH_2)_{0-3}-NR12-(CH_2)_{1-3}-C(=O)-A$;
and A is a 6- to 12- membered bicyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein the bicyclic ring system is fused, bridged or spiro; X is CH_2 and Y is NH; and B is heteroaryl[a] and selected from isoquinolinyl and azaindole (specifically 7-azaindole), optionally substituted as for heteroaryl[a].

More specifically, -V-Z- is selected from $-CH_2-$, $-O-CH_2-$, $-CH_2-O-$, $-CH_2-CH_2-O-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$, wherein R18 is selected from:



AW- is selected from:

$-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and $-(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 6- to 12- membered bicyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein the bicyclic ring system is fused, bridged or spiro; X is CH_2 and Y is NH; and B is heteroaryl[a] and selected from isoquinolinyl and azaindole (specifically 7-azaindole), optionally substituted as for heteroaryl[a].

More specifically, -V-Z- is selected from $-CH_2-$, $-O-CH_2-$, $-CH_2-O-$ and $-CH_2-CH_2-O-$;

AW- is selected from:

$-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and $-(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 6- to 12- membered bicyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein the bicyclic ring system is fused, bridged or spiro; X is CH_2 and Y is NH; and B is heteroaryl[a] and selected from isoquinolinyl and azaindole (specifically 7-azaindole), optionally substituted as for heteroaryl[a].

More specifically, AW- is selected from:

$-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and $-(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 6- to 12- membered bicyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein the bicyclic ring system is fused, bridged or spiro; X is CH_2 and Y is NH; and B is heteroaryl[a] and selected from isoquinolinyl and azaindole (specifically 7-azaindole), optionally substituted as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: $-CH_2$-, -O-CH_2-, -O-$C(CH_3)_2$-, $-CH_2$-O-, $-C(CH_3)_2$-O-, -NH-CH_2-, $-CH_2$-NH-, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2$-, -O-CH_2-CH_2, $-CH_2$-O-CH_2, $-CH_2-CH_2$-O-, $-CH_2-CH_2-CH_2$- $-CH_2$-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2$-;

AW- is selected from:

$-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-A, $-(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and $-(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one further ring member independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl; and X is CH_2 and Y is NH or N; and B is heteroaryl[a] and selected from isoquinolinyl and azaindole (specifically 7-azaindole), optionally substituted as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: $-CH_2$-, -O-CH_2-, -O-$C(CH_3)_2$-, $-CH_2$-O-, $-C(CH_3)_2$-O-, -NH-CH_2-, $-CH_2$-NH-, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2$-, -O-CH_2-CH_2, $-CH_2-CH_2$-O-, $-CH_2-CH_2-CH_2$- $-CH_2$-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one further ring member independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl; and X is CH_2 and Y is NH or N; and B is heteroaryl[a] and selected from isoquinolinyl and azaindole (specifically 7-azaindole), optionally substituted as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one further ring member independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl; and X is CH_2 and Y is NH or N; and B is heteroaryl[a] and selected from isoquinolinyl and azaindole (specifically 7-azaindole), optionally substituted as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

$-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-O-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-NH-(CH_2)_{0-3}-A$ and $-(CH_2)_{0-3}-NR12-(CH_2)_{1-3}-C(=O)-A$; and A is a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one further ring member independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl; and X is CH_2 and Y is NH; X is CH_2 and Y is NH; and B is heteroaryl[a] and selected from isoquinolinyl and azaindole (specifically 7-azaindole), optionally substituted as for heteroaryl[a].

Alternatively, -V-Z- is selected from $-CH_2-$, $-O-CH_2-$, $-CH_2-O-$, $-CH_2-CH_2-O-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

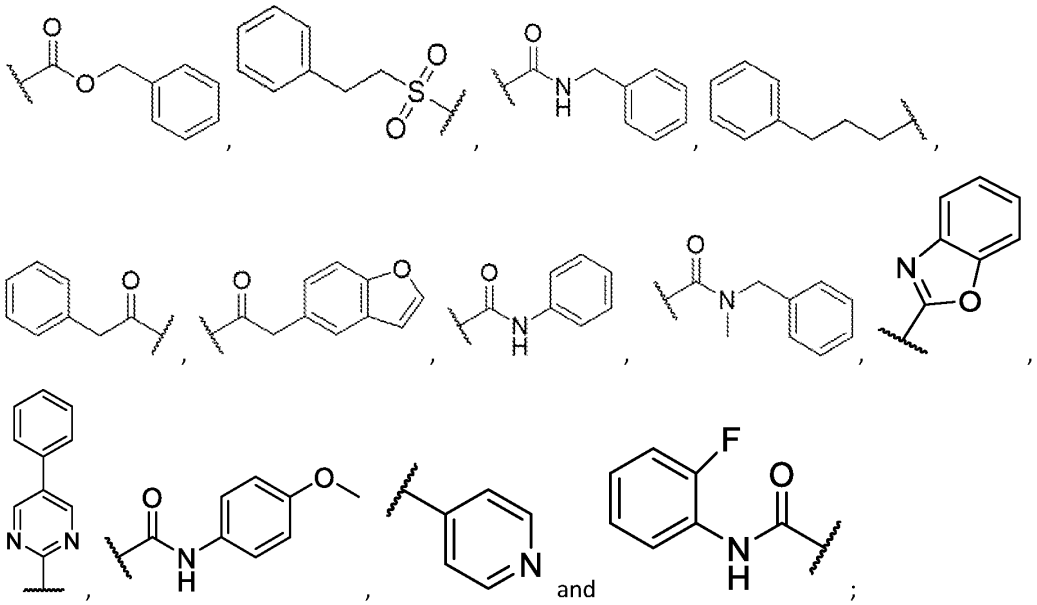
wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

$-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-O-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-A$, $-(CH_2)_{0-3}-NH-(CH_2)_{0-3}-A$ and $-(CH_2)_{0-3}-NR12-(CH_2)_{1-3}-C(=O)-A$; and A is a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one further ring member independently selected from N, optionally wherein the ring system is

substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl; and X is CH_2 and Y is NH; X is CH_2 and Y is NH; and B is heteroaryl[a] and selected from isoquinolinyl and azaindole (specifically 7-azaindole), optionally substituted as for heteroaryl[a].

Alternatively, -V-Z- is selected from from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



AW- is selected from:

-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one further ring member independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl; and X is CH_2 and Y is NH; X is CH_2 and Y is NH; and B is heteroaryl[a] and selected from isoquinolinyl and azaindole (specifically 7-azaindole), optionally substituted as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one further ring member independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl; and X is CH_2 and Y is NH; X is CH_2 and Y is NH; and B is heteroaryl[a] and selected from isoquinolinyl and azaindole (specifically 7-azaindole), optionally substituted as for heteroaryl[a].

Alternatively, AW- is selected from:

-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-A, -$(CH_2)_{0-3}$-NH-$(CH_2)_{0-3}$-A and -$(CH_2)_{0-3}$-NR12-$(CH_2)_{1-3}$-C(=O)-A; and A is a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl. A can be a 4- to 7- membered monocyclic ring system, containing one N ring member and optionally one further ring member independently selected from N, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from alkyl and cycloalkyl; and X is CH_2 and Y is NH; X is CH_2 and Y is NH; and B is heteroaryl[a] and selected from isoquinolinyl and azaindole (specifically 7-azaindole), optionally substituted as for heteroaryl[a].

More preferably, AW- is selected from:

-$(CHR12)_{0-6}$-A (e.g. -$(CHR12)_{0-3}$-A, specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected

from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is NH or N; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or

10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is NH or N; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is NH or N; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is NH or N; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is NH or N; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo,

alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is NH or N; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

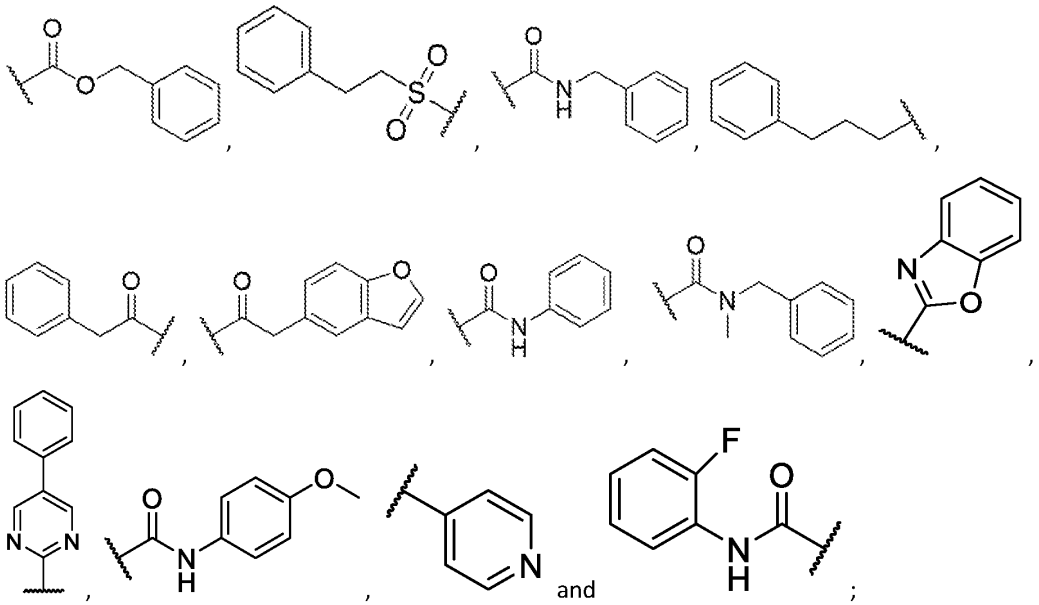
$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

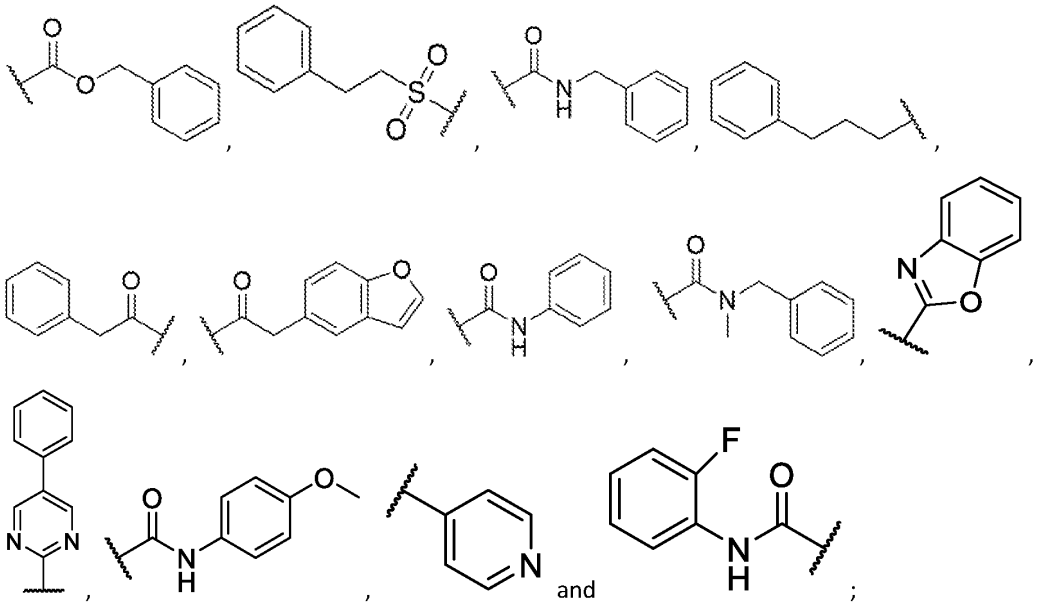
More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or

both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a]. Alternatively, AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13,

C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is NH or N; and B is heteroaryl[a], specifically isoquinolinyl substituted with –NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12,

C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is NH or N; and B is heteroaryl[a], specifically isoquinolinyl substituted with $–NH_2$, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;
AW- is selected from:
-(CHR12)-A (specifically $–(CH_2)$-A) and $-(CH_2)_{0-6}-O-(CH_2)_{0-6}$-A (e.g. $-(CH_2)_{0-3}-O-(CH_2)_{0-3}$-A, specifically $–(CH_2)$-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is NH or N; and B is heteroaryl[a], specifically isoquinolinyl substituted with $–NH_2$, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;
AW- is selected from:
-(CHR12)-A (specifically $–(CH_2)$-A) and $-(CH_2)_{0-6}-O-(CH_2)_{0-6}$-A (e.g. $-(CH_2)_{0-3}-O-(CH_2)_{0-3}$-A, specifically $–(CH_2)$-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically isoquinolinyl substituted with $–NH_2$, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

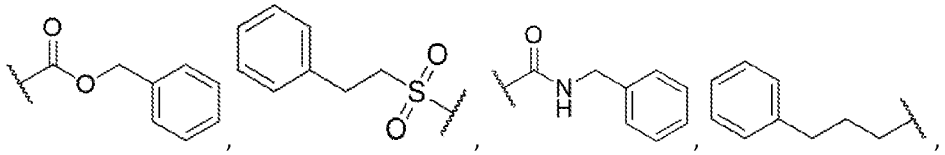
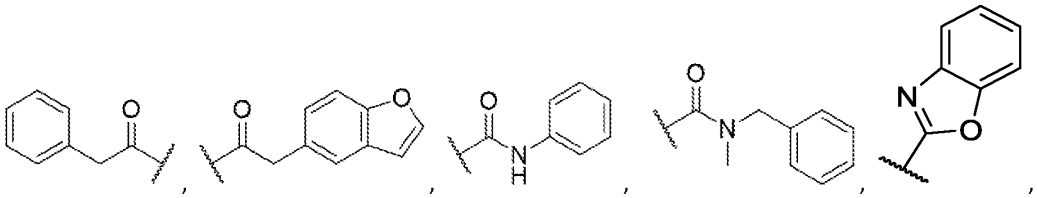
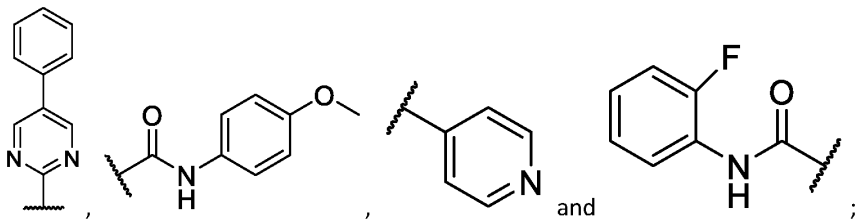
$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically isoquinolinyl substituted with –NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:




and ;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring

member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically isoquinolinyl substituted with $–NH_2$, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;
AW- is selected from:
-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically isoquinolinyl substituted with $–NH_2$, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

More preferably, AW- is selected from:
-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically isoquinolinyl substituted with $–NH_2$, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-,

$-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

AW- is selected from:

-(CHR12)-A (specifically $-(CH_2)$-A), $-(CH_2)_{0-6}-C(=O)-(CH_2)_{0-6}$-A (e.g. $-(CH_2)_{0-3}-C(=O)-(CH_2)_{0-3}$-A , specifically $-C(=O)$-A) and $-(CH_2)_{0-6}-O-(CH_2)_{0-6}$-A (e.g. $-(CH_2)_{0-3}-O-(CH_2)_{0-3}$-A, specifically $-(CH_2)-O$-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is O; and B is heteroaryl[a], specifically isoquinolinyl substituted with$-NH_2$, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

AW- is selected from:

-(CHR12)-A (specifically $-(CH_2)$-A), $-(CH_2)_{0-6}-C(=O)-(CH_2)_{0-6}$-A (e.g. $-(CH_2)_{0-3}-C(=O)-(CH_2)_{0-3}$-A , specifically $-C(=O)$-A) and $-(CH_2)_{0-6}-O-(CH_2)_{0-6}$-A (e.g. $-(CH_2)_{0-3}-O-(CH_2)_{0-3}$-A, specifically $-(CH_2)-O$-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is O; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$,

$-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

AW- is selected from:

-(CHR12)-A (specifically $-(CH_2)-A$), $-(CH_2)_{0-6}-C(=O)-(CH_2)_{0-6}-A$ (e.g. $-(CH_2)_{0-3}-C(=O)-(CH_2)_{0-3}-A$, specifically $-C(=O)-A$) and $-(CH_2)_{0-6}-O-(CH_2)_{0-6}-A$ (e.g. $-(CH_2)_{0-3}-O-(CH_2)_{0-3}-A$, specifically $-(CH_2)-O-A$); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is O; and B is heteroaryl[a], specifically isoquinolinyl substituted with$-NH_2$, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

AW- is selected from:

-(CHR12)-A (specifically $-(CH_2)-A$), $-(CH_2)_{0-6}-C(=O)-(CH_2)_{0-6}-A$ (e.g. $-(CH_2)_{0-3}-C(=O)-(CH_2)_{0-3}-A$, specifically $-C(=O)-A$) and $-(CH_2)_{0-6}-O-(CH_2)_{0-6}-A$ (e.g. $-(CH_2)_{0-3}-O-(CH_2)_{0-3}-A$, specifically $-(CH_2)-O-A$); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is O; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is O; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is O; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or

10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is O; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

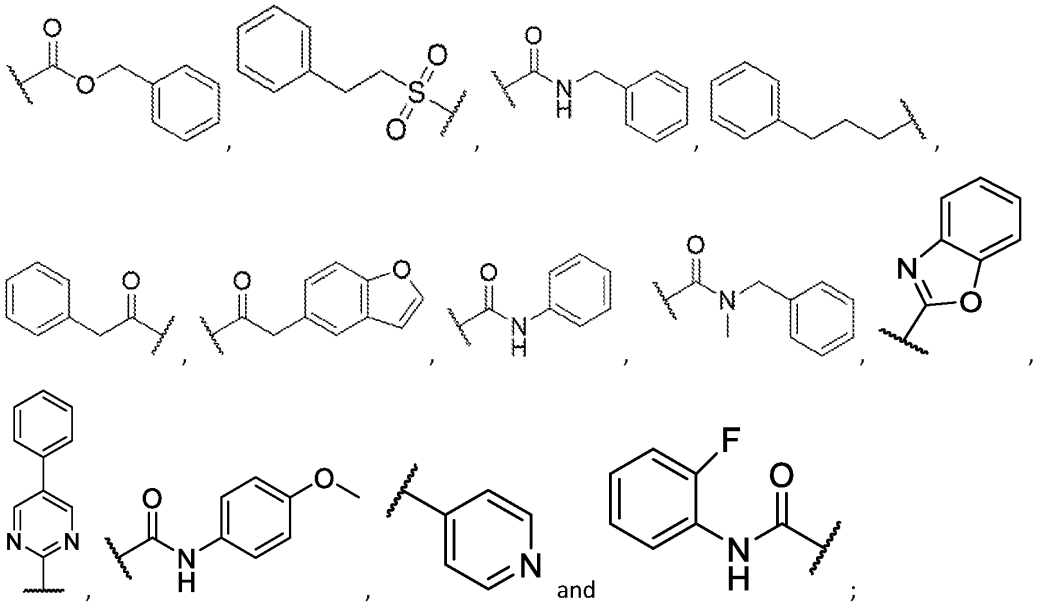
$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is O; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

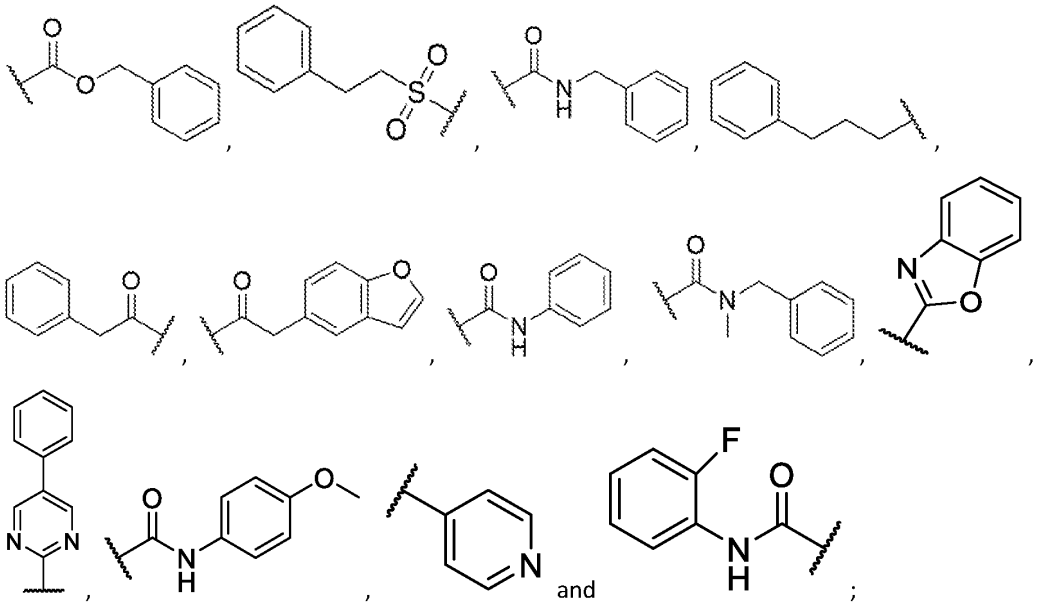
More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is O; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is O; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or

both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is O; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is O; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is O; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a]. Alternatively, AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13,

C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is O; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is O; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is O; and B is

heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

AW- is selected from:

-(CHR12)-A (specifically $-(CH_2)$-A) and $-(CH_2)_{0-6}-O-(CH_2)_{0-6}$-A (e.g. $-(CH_2)_{0-3}-O-(CH_2)_{0-3}$-A, specifically $-(CH_2)$-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is O; and B is heteroaryl[a], specifically isoquinolinyl substituted with$-NH_2$, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

AW- is selected from:

-(CHR12)-A (specifically $-(CH_2)$-A) and $-(CH_2)_{0-6}-O-(CH_2)_{0-6}$-A (e.g. $-(CH_2)_{0-3}-O-(CH_2)_{0-3}$-A, specifically $-(CH_2)$-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is O; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is O; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is O; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is O; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

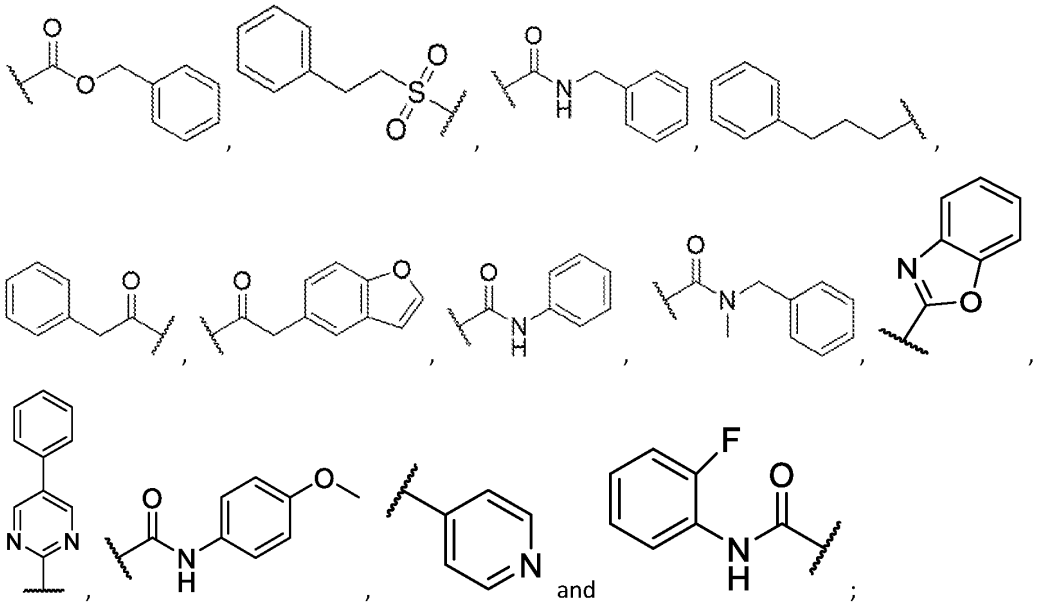
$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is O; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

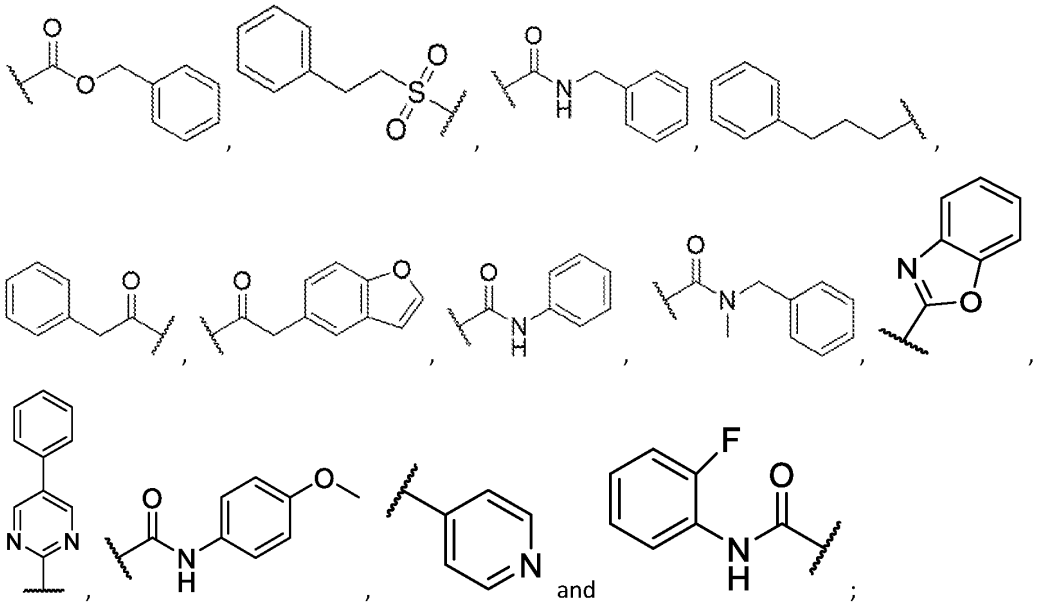
More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is O; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is O; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is O; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as

for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is O; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is O; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a]. Alternatively, AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 9- or 10- membered bicyclic ring system (particularly 9-membered) containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; wherein one of the rings in the bicyclic ring system can be aromatic or both of the rings in the bicyclic ring system can be aromatic; X is CH_2 and Y is O; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

-(CHR12)-A (specifically $-(CH_2)-A$), $-(CH_2)_{0-6}-C(=O)-(CH_2)_{0-6}-A$ (e.g. $-(CH_2)_{0-3}-C(=O)-(CH_2)_{0-3}-A$, specifically $-C(=O)-A$) and $-(CH_2)_{0-6}-O-(CH_2)_{0-6}-A$ (e.g. $-(CH_2)_{0-3}-O-(CH_2)_{0-3}-A$, specifically $-(CH_2)-O-A$); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH or N; and B is heteroaryl[a], specifically isoquinolinyl substituted with$-NH_2$, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

-(CHR12)-A (specifically $-(CH_2)-A$), $-(CH_2)_{0-6}-C(=O)-(CH_2)_{0-6}-A$ (e.g. $-(CH_2)_{0-3}-C(=O)-(CH_2)_{0-3}-A$, specifically $-C(=O)-A$) and $-(CH_2)_{0-6}-O-(CH_2)_{0-6}-A$ (e.g. $-(CH_2)_{0-3}-O-(CH_2)_{0-3}-A$, specifically $-(CH_2)-O-A$); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH or N; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole),), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$,

$-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

-(CHR12)-A (specifically $-(CH_2)$-A), $-(CH_2)_{0-6}-C(=O)-(CH_2)_{0-6}$-A (e.g. $-(CH_2)_{0-3}-C(=O)-(CH_2)_{0-3}$-A , specifically –C(=O)-A) and $-(CH_2)_{0-6}-O-(CH_2)_{0-6}$-A (e.g. $-(CH_2)_{0-3}-O-(CH_2)_{0-3}$-A, specifically $-(CH_2)-O$-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH or N; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

-(CHR12)-A (specifically $-(CH_2)$-A), $-(CH_2)_{0-6}-C(=O)-(CH_2)_{0-6}$-A (e.g. $-(CH_2)_{0-3}-C(=O)-(CH_2)_{0-3}$-A , specifically –C(=O)-A) and $-(CH_2)_{0-6}-O-(CH_2)_{0-6}$-A (e.g. $-(CH_2)_{0-3}-O-(CH_2)_{0-3}$-A, specifically $-(CH_2)-O$-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH or N; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole),), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH or N; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH or N; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole),), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole),), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

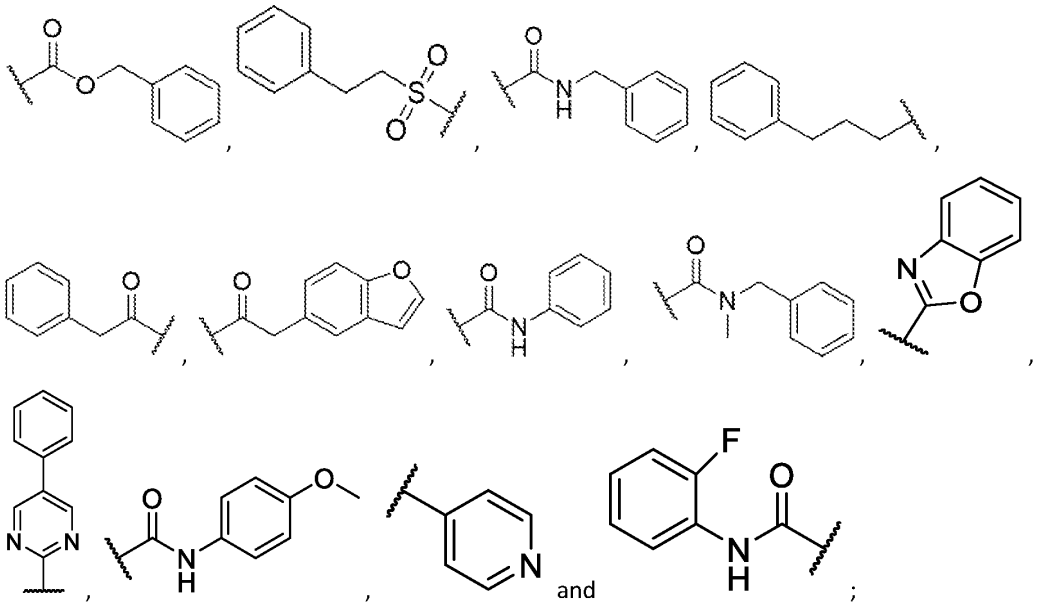
$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole),), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

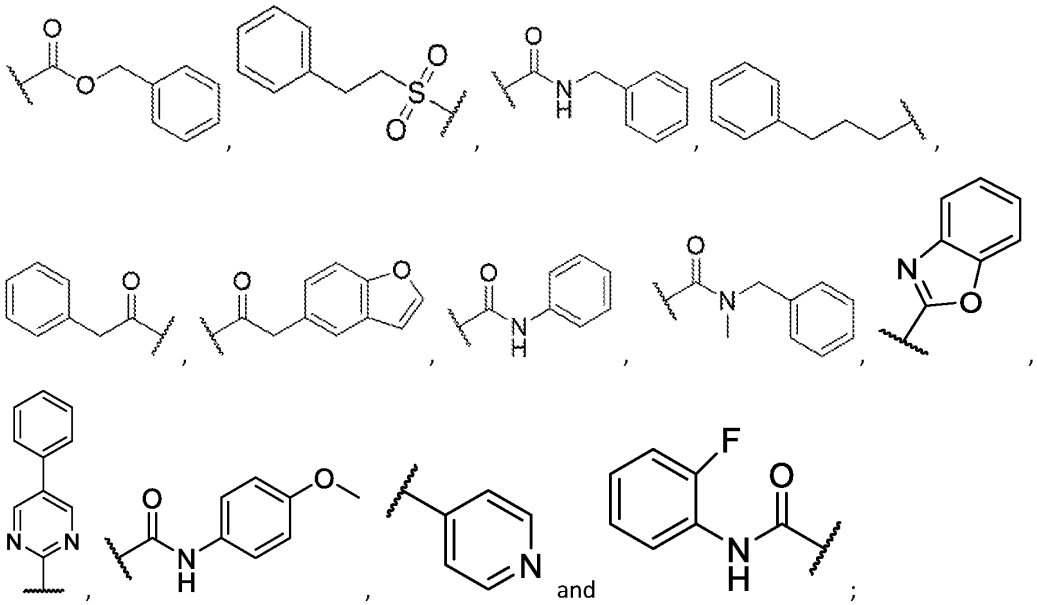
More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole),), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is

heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole),), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a]. Alternatively, AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole),), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is NH or N; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is NH or N; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is NH or N; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is NH or N; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is NH or N; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

-(CHR12)-A (specifically $-(CH_2)-A$) and $-(CH_2)_{0-6}-O-(CH_2)_{0-6}-A$ (e.g. $-(CH_2)_{0-3}-O-(CH_2)_{0-3}-A$, specifically $-(CH_2)-O-A$); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is NH or N; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

-(CHR12)-A (specifically $-(CH_2)-A$) and $-(CH_2)_{0-6}-O-(CH_2)_{0-6}-A$ (e.g. $-(CH_2)_{0-3}-O-(CH_2)_{0-3}-A$, specifically $-(CH_2)-O-A$); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically isoquinolinyl substituted with$-NH_2$, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

-(CHR12)-A (specifically $-(CH_2)-A$) and $-(CH_2)_{0-6}-O-(CH_2)_{0-6}-A$ (e.g. $-(CH_2)_{0-3}-O-(CH_2)_{0-3}-A$, specifically $-(CH_2)-O-A$); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

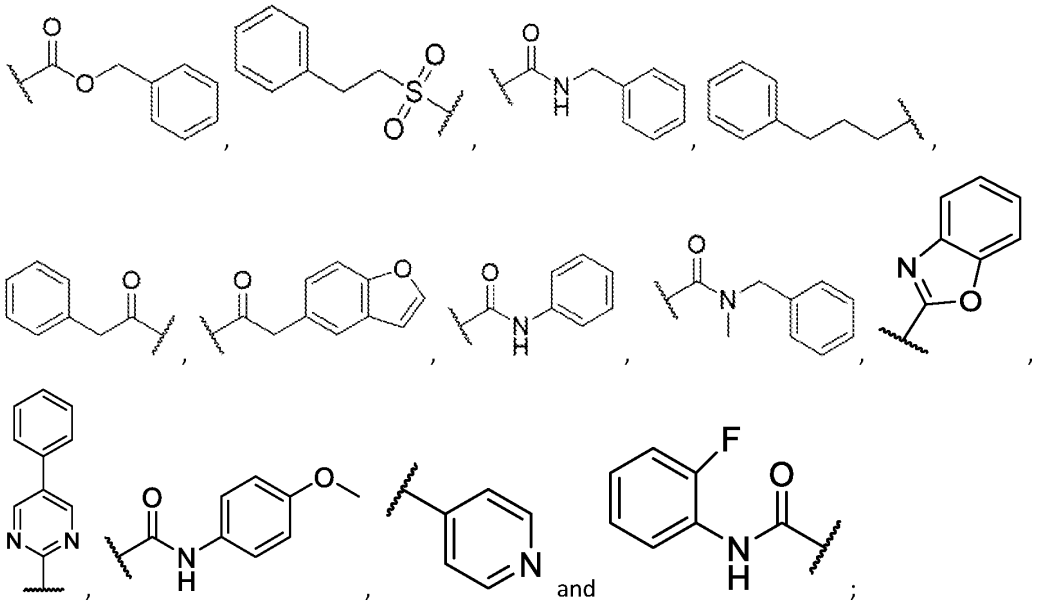
$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



, wherein R18 is selected from:

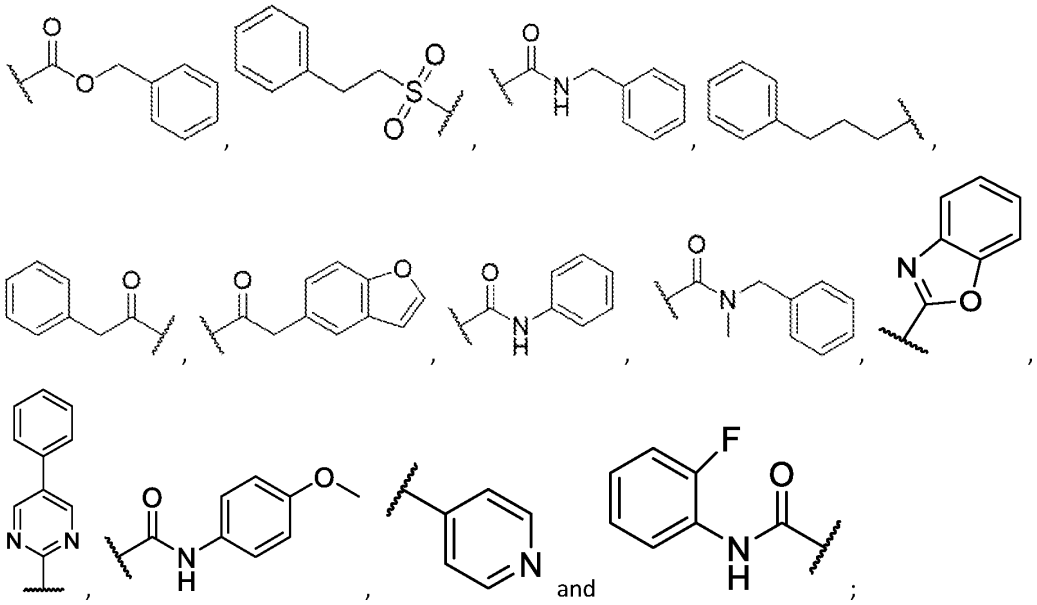
$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, AW- is selected from:
-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a]. Alternatively, AW- is selected from:
-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is NH; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;
AW- is selected from:
-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is

substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH or N; X is CH_2 and Y is O; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH or N; X is CH_2 and Y is O; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH or N; X is CH_2 and Y is O; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is

heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$ $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

-(CHR12)-A (specifically $-(CH_2)-A$), $-(CH_2)_{0-6}-C(=O)-(CH_2)_{0-6}-A$ (e.g. $-(CH_2)_{0-3}-C(=O)-(CH_2)_{0-3}-A$, specifically $-C(=O)-A$) and $-(CH_2)_{0-6}-O-(CH_2)_{0-6}-A$ (e.g. $-(CH_2)_{0-3}-O-(CH_2)_{0-3}-A$, specifically $-(CH_2)-O-A$); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH or N; X is CH_2 and Y is O; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

-(CHR12)-A (specifically $-(CH_2)-A$), $-(CH_2)_{0-6}-C(=O)-(CH_2)_{0-6}-A$ (e.g. $-(CH_2)_{0-3}-C(=O)-(CH_2)_{0-3}-A$, specifically $-C(=O)-A$) and $-(CH_2)_{0-6}-O-(CH_2)_{0-6}-A$ (e.g. $-(CH_2)_{0-3}-O-(CH_2)_{0-3}-A$, specifically $-(CH_2)-O-A$); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is O; and B is heteroaryl[a], specifically isoquinolinyl substituted with$-NH_2$, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: $-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or, when -V-Z- is absent: U is absent, CH_2 or $-CH_2CH_2-$;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is O; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is O; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

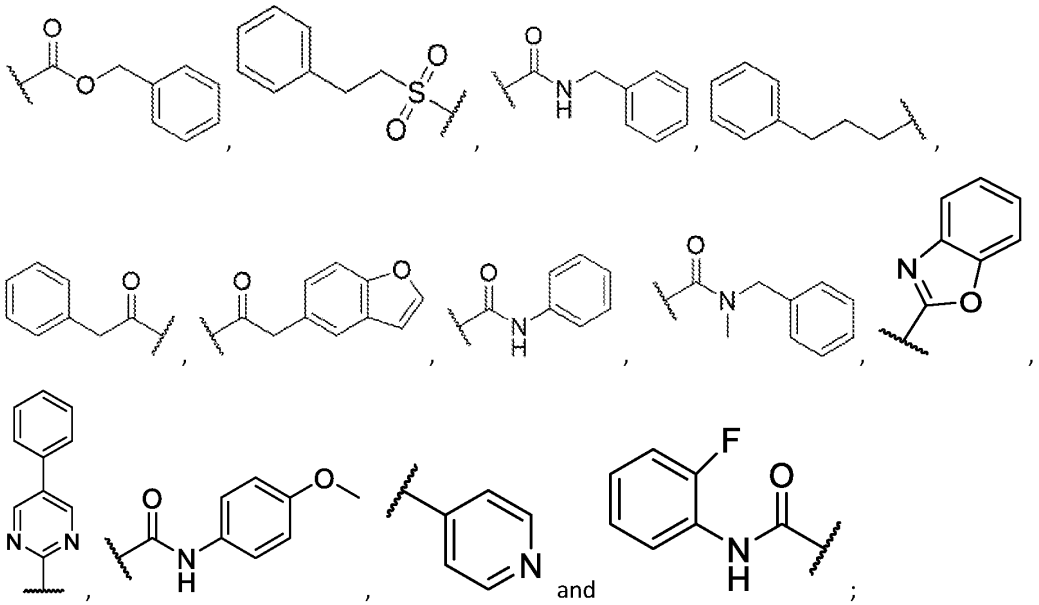
wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14,

NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is O; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

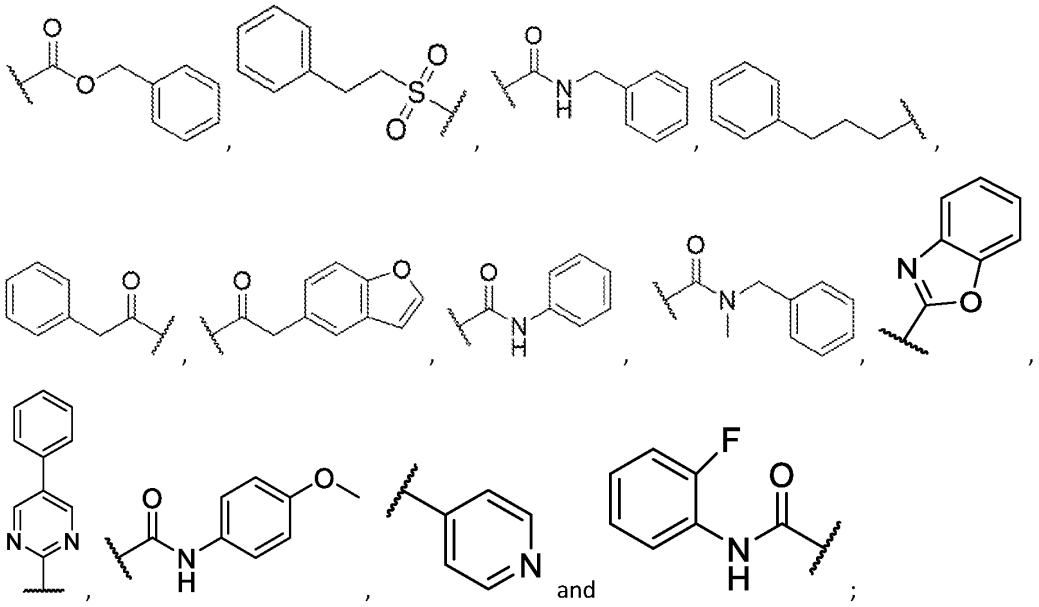
More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is O; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is O; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is O; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is O; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is O; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a]. Alternatively, AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A), -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-C(=O)-$(CH_2)_{0-3}$-A , specifically –C(=O)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is O; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH or N; X is CH_2 and Y is O; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH or N; X is CH_2 and Y is O; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH or N; X is CH_2 and Y is O; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2- -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from: $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19; wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH or N; X is CH_2 and Y is O; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -N($COCH_3$)-CH_2, -CH_2-N($COCH_3$), -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is O; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, when not absent, -V-Z- is selected from: -CH_2-, -O-CH_2-, -O-$C(CH_3)_2$-, -CH_2-O-, -$C(CH_3)_2$-O-, -NH-CH_2-, -CH_2-NH-, -$N(COCH_3)$-CH_2, -CH_2-$N(COCH_3)$, -CH_2-CH_2-, -O-CH_2-CH_2, -CH_2-O-CH_2, -CH_2-CH_2-O-, and -CH_2-CH_2-CH_2-; or, when -V-Z- is absent: U is absent, CH_2 or -CH_2CH_2-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is O; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is O; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

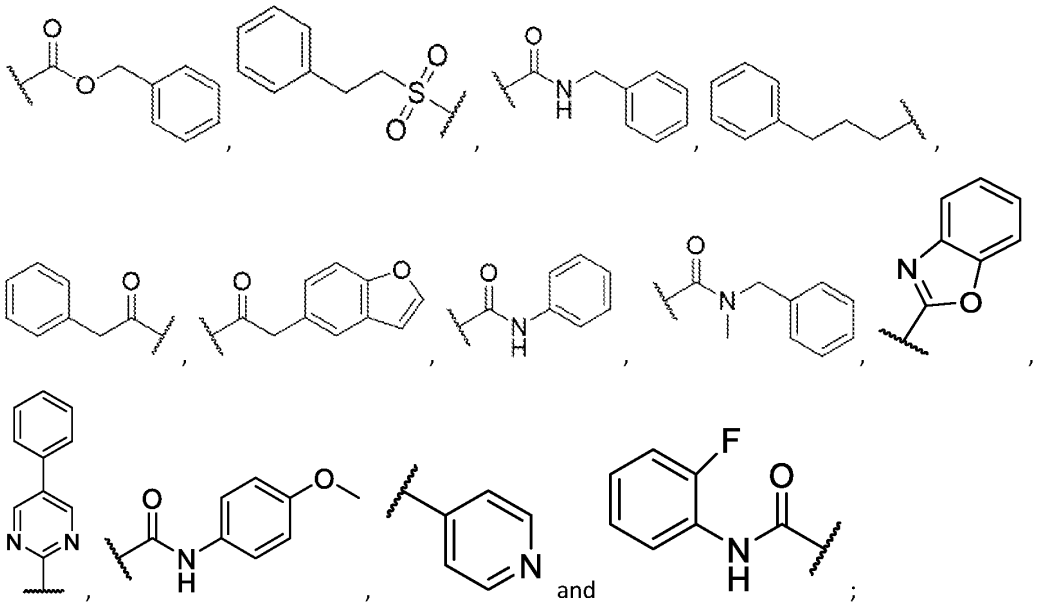
wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a] ;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from

halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is O; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

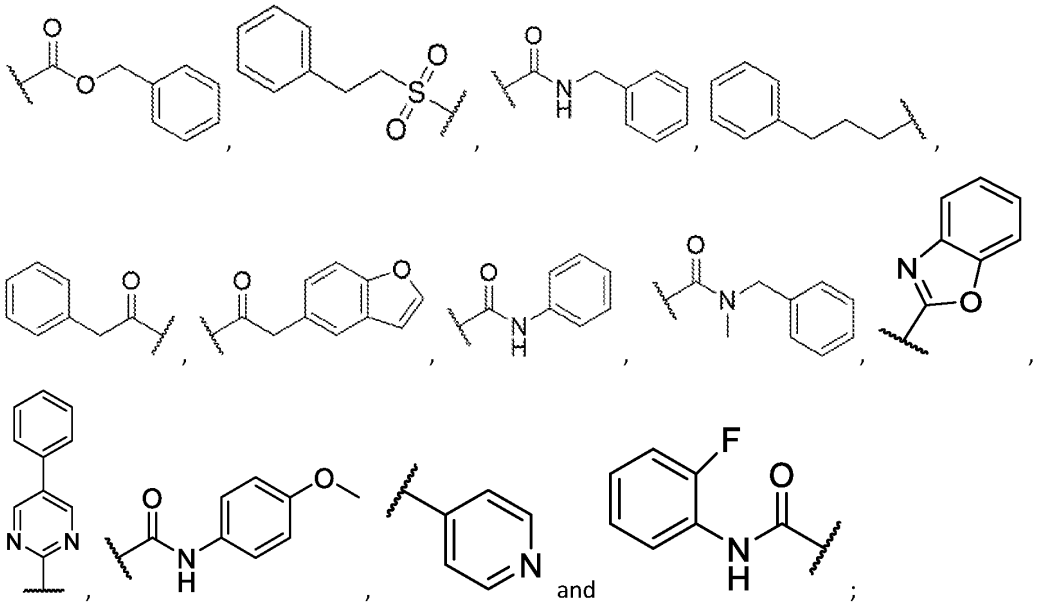
More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is O; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-, wherein R18 is selected from:



AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is O; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is O; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a].

Alternatively, -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-;

AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is O; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

More preferably, AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is O; and B is heteroaryl[a], specifically isoquinolinyl substituted with–NH_2, and optionally 1 or 2 further substituent as for heteroaryl[a], or B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with halo (particularly, chloro), and optionally 1 or 2 further substituent as for heteroaryl[a]. Alternatively, , AW- is selected from:

-(CHR12)-A (specifically –(CH_2)-A) and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A (e.g. -$(CH_2)_{0-3}$-O-$(CH_2)_{0-3}$-A, specifically –(CH_2)-O-A); and A is a 6-membered monocyclic ring system containing one N ring member, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN; and X is CH_2 and Y is NH; X is CH_2 and Y is O; and B is heteroaryl[a], specifically azaindole (particularly 7-azaindole), substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

For the compounds provided in Table 1a, Table 1b, Table 2a, Table 2b, Table 3a, Table 4a, Table 5b, Table 6a, Table 6b, Table 7a, Table 7b, Table 8a, Table 8b, Table 9b, Table 10a, Table 10b, Table 11b, Table 12b and Table 13b below, where stereochemistry is indicated, the compound is intended to cover all possible stereoisomers thereof.

The present invention therefore provides the compounds below in Table 1a, and pharmaceutically acceptable salts and/or solvates thereof. The present invention therefore also provides stereoisomers of the compounds below in Table 1a, and pharmaceutically acceptable salts and/or solvates thereof.

The present invention therefore provides the compounds below in Table 2a, and pharmaceutically acceptable salts and/or solvates thereof. The present invention therefore also provides stereoisomers of the compounds below in Table 2a, and pharmaceutically acceptable salts and/or solvates thereof.

The present invention therefore provides the compounds below in Table 2b, and pharmaceutically acceptable salts and/or solvates thereof. The present invention therefore also provides stereoisomers of the compounds below in Table 2b, and pharmaceutically acceptable salts and/or solvates thereof.

The present invention therefore provides the compounds below in Table 3a, and pharmaceutically acceptable salts and/or solvates thereof. The present invention therefore also provides stereoisomers of the compounds below in Table 3a, and pharmaceutically acceptable salts and/or solvates thereof.

The present invention therefore provides the compounds below in Table 4a, and pharmaceutically acceptable salts and/or solvates thereof. The present invention therefore also provides stereoisomers of the compounds below in Table 4a, and pharmaceutically acceptable salts and/or solvates thereof.

The present invention therefore provides the compounds below in Table 5b, and pharmaceutically acceptable salts and/or solvates thereof. The present invention therefore also provides stereoisomers of the compounds below in Table 5b, and pharmaceutically acceptable salts and/or solvates thereof.

The present invention therefore provides the compounds below in Table 6a, and pharmaceutically acceptable salts and/or solvates thereof. The present invention therefore also provides stereoisomers of the compounds below in Table 6a, and pharmaceutically acceptable salts and/or solvates thereof.

The present invention therefore provides the compounds below in Table 6b, and pharmaceutically acceptable salts and/or solvates thereof. The present invention therefore also provides stereoisomers of the compounds below in Table 6b, and pharmaceutically acceptable salts and/or solvates thereof.

The present invention therefore provides the compounds below in Table 7a, and pharmaceutically acceptable salts and/or solvates thereof. The present invention therefore also provides stereoisomers of the compounds below in Table 7a, and pharmaceutically acceptable salts and/or solvates thereof.

The present invention therefore provides the compounds below in Table 7b, and pharmaceutically acceptable salts and/or solvates thereof. The present invention therefore also provides stereoisomers of the compounds below in Table 7b, and pharmaceutically acceptable salts and/or solvates thereof.

The present invention therefore provides the compounds below in Table 8a, and pharmaceutically acceptable salts and/or solvates thereof. The present invention therefore also provides stereoisomers of the compounds below in Table 8a, and pharmaceutically acceptable salts and/or solvates thereof.

The present invention therefore provides the compounds below in Table 8b, and pharmaceutically acceptable salts and/or solvates thereof. The present invention therefore also provides stereoisomers of the compounds below in Table 8b, and pharmaceutically acceptable salts and/or solvates thereof.

The present invention therefore provides the compounds below in Table 9b, and pharmaceutically acceptable salts and/or solvates thereof. The present invention therefore also provides stereoisomers of the compounds below in Table 9b, and pharmaceutically acceptable salts and/or solvates thereof.

The present invention therefore provides the compounds below in Table 10a, and pharmaceutically acceptable salts and/or solvates thereof. The present invention therefore also provides stereoisomers of the compounds below in Table 10a, and pharmaceutically acceptable salts and/or solvates thereof.

The present invention therefore provides the compounds below in Table 10b, and pharmaceutically acceptable salts and/or solvates thereof. The present invention therefore also provides stereoisomers of the compounds below in Table 10b, and pharmaceutically acceptable salts and/or solvates thereof.

The present invention therefore provides the compounds below in Table 11b, and pharmaceutically acceptable salts and/or solvates thereof. The present invention therefore also provides stereoisomers of the compounds below in Table 11b, and pharmaceutically acceptable salts and/or solvates thereof.

The present invention therefore provides the compounds below in Table 12b, and pharmaceutically acceptable salts and/or solvates thereof. The present invention therefore also provides stereoisomers of the compounds below in Table 12b, and pharmaceutically acceptable salts and/or solvates thereof.

The present invention therefore provides the compounds below in Table 13b, and pharmaceutically acceptable salts and/or solvates thereof. The present invention therefore also provides stereoisomers of the compounds below in Table 13b, and pharmaceutically acceptable salts and/or solvates thereof.

It will be understood that, when reading the compounds in Table 1a, Table 1b, Table 2a, Table 2b, Table 3a, Table 4a, Table 5b, Table 6a, Table 6b, Table 7a, Table 7b, Table 8a, Table 8b, Table 9b, Table 10a, Table 10b, Table 11b, Table 12b and Table 13b below, the substituents are to be read from left to right.

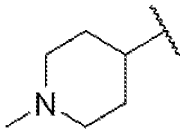
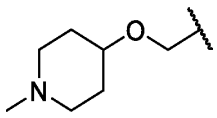
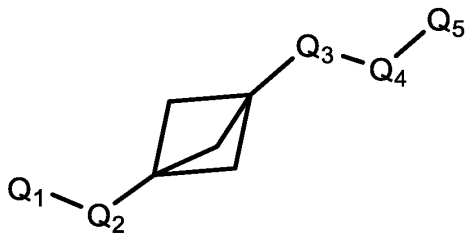
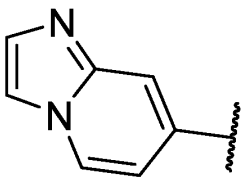
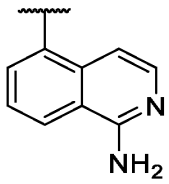
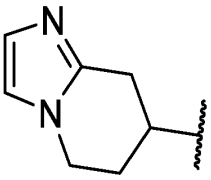
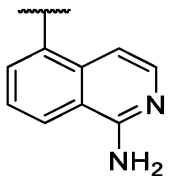
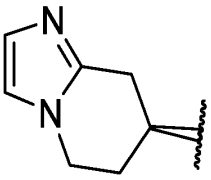
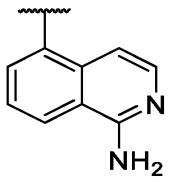
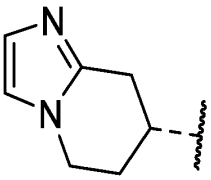
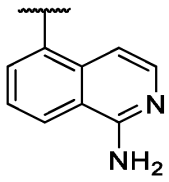
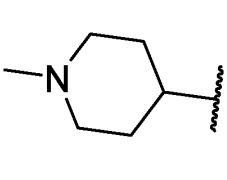
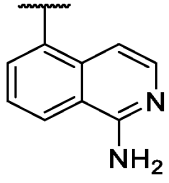
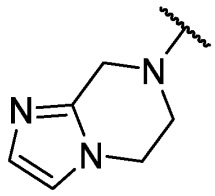
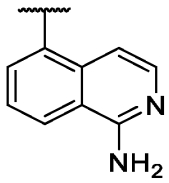
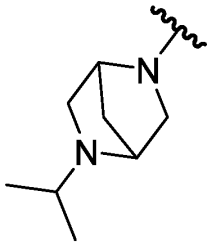
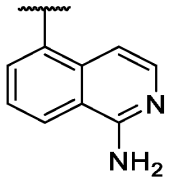
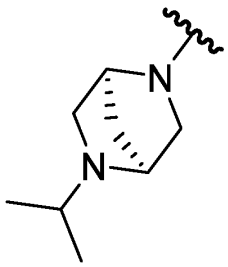
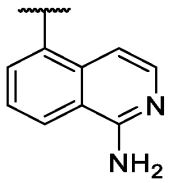
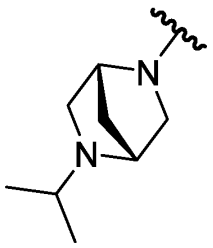
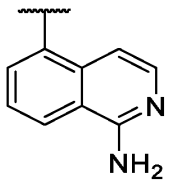
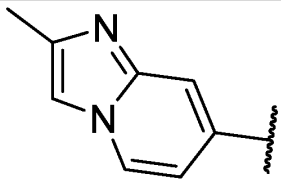
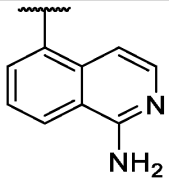
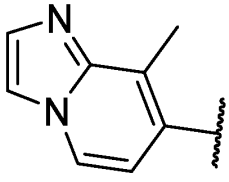
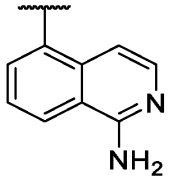
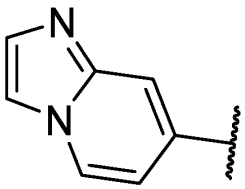
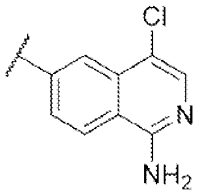
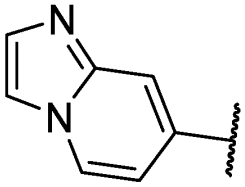
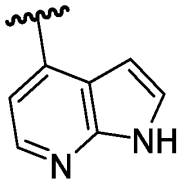
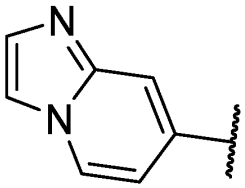
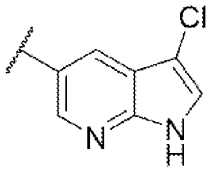
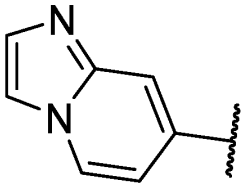
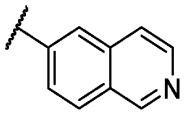
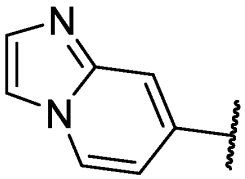
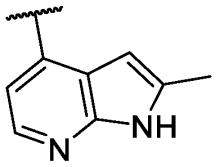
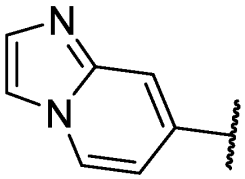
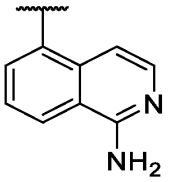
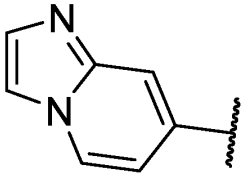
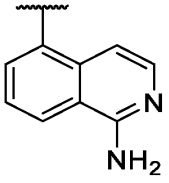
For example, example compound 1003 in Table 1a has a Q_1 group:  and a Q_2 group "OCH_2". Therefore, the Q_1 group is attached to the "O" of the "OCH_2" of the Q_2 group, as follows:  .

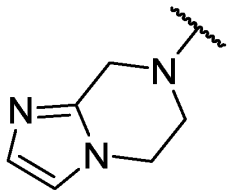
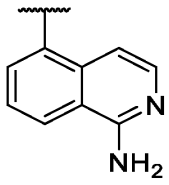
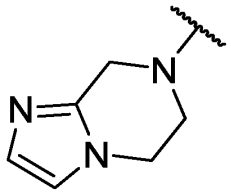
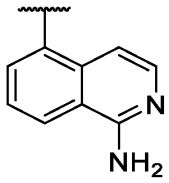
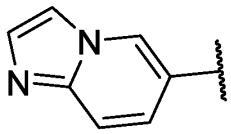
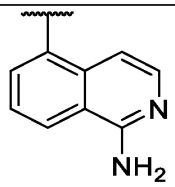
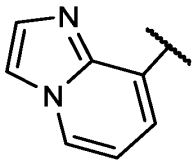
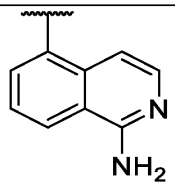
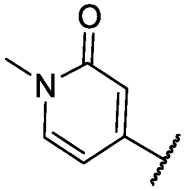
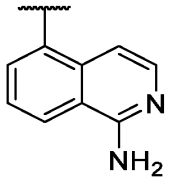
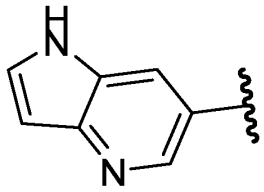
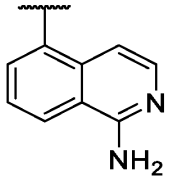
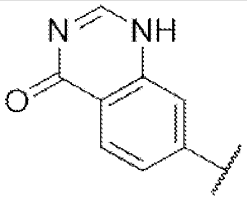
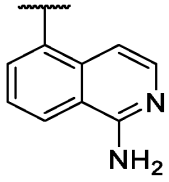
Table 1a

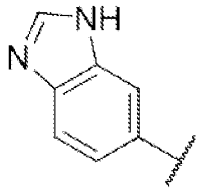
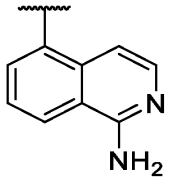
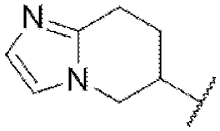
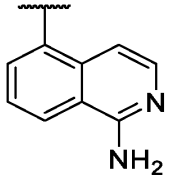
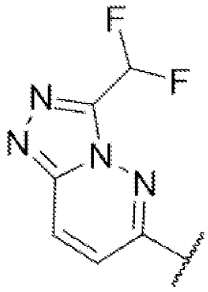
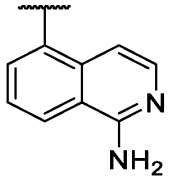
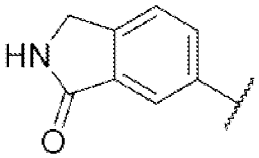
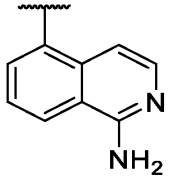
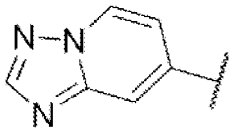
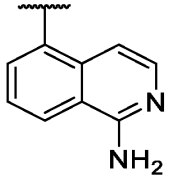
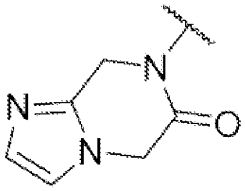
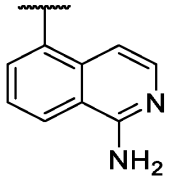


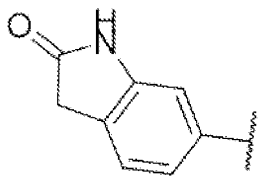
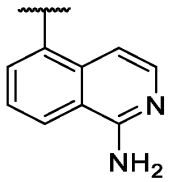
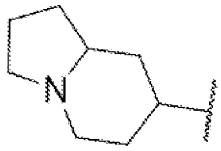
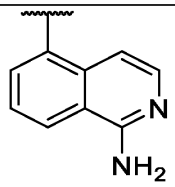
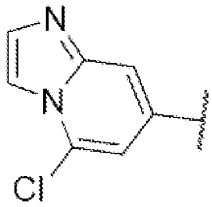
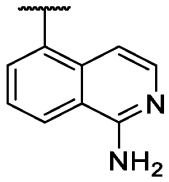
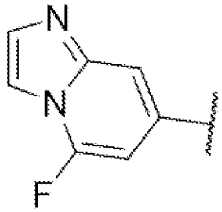
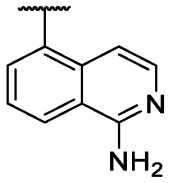
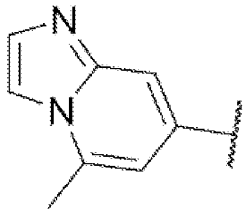
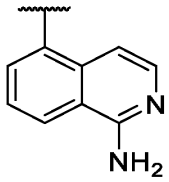
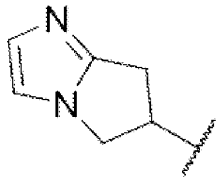
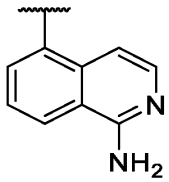
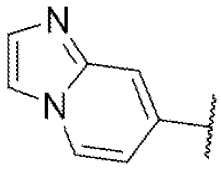
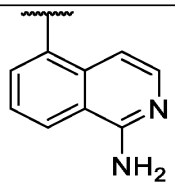
Example No	Q_1	Q_2	Q_3	Q_4	Q_5
1001		OCH_2	CH_2	NH	
1002		OCH_2	CH_2	NH	
1002.1		OCH_2	CH_2	NH	
1002.2		OCH_2	CH_2	NH	
1003		OCH_2	CH_2	NH	

Example No	Q_1	Q_2	Q_3	Q_4	Q_5
1004		CH_2	CH_2	NH	
1005		CH_2	CH_2	NH	
1005.1		CH_2	CH_2	NH	
1005.2		CH_2	CH_2	NH	
1006		OCH_2	CH_2	NH	
1007		OCH_2	CH_2	NH	

Example No	Q_1	Q_2	Q_3	Q_4	Q_5
1008		OCH_2	CH_2	NH	
1009		OCH_2	CH_2	NH	
1010		OCH_2	CH_2	NH	
1011		OCH_2	CH_2	NH	
1012		OCH_2	CH_2	NH	
1013		OCH_2	CH_2	O	
1014		OCH_2	CH_2	CH_2	

Example No	Q_1	Q_2	Q_3	Q_4	Q_5
1015		C=O	CH_2	O	
1016		C=O	CH_2	NH	
1017		OCH_2	CH_2	NH	
1018		OCH_2	CH_2	NH	
1019		OCH_2	CH_2	NH	
1101		OCH_2	CH_2	NH	
1104		OCH_2	CH_2	NH	

Example No	Q_1	Q_2	Q_3	Q_4	Q_5
1105		OCH_2	CH_2	NH	
1106		OCH_2	CH_2	NH	
1108		OCH_2	CH_2	NH	
1109		OCH_2	CH_2	NH	
1110		OCH_2	CH_2	NH	
1112		CH_2	CH_2	NH	

Example No	Q_1	Q_2	Q_3	Q_4	Q_5
1113		OCH_2	CH_2	NH	
1114		OCH_2	CH_2	NH	
1115		OCH_2	CH_2	NH	
1116		OCH_2	CH_2	NH	
1117		OCH_2	CH_2	NH	
1118		OCH_2	CH_2	NH	
1119		CH_2O	CH_2	NH	

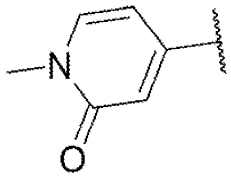
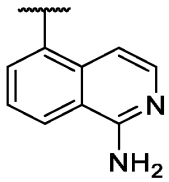
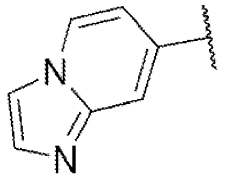
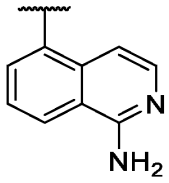
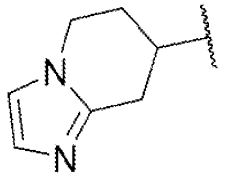
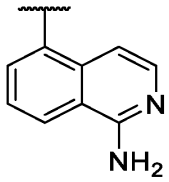
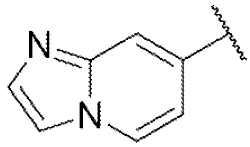
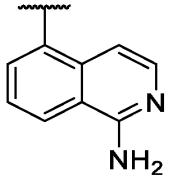
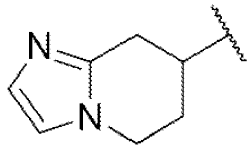
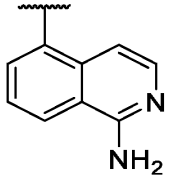
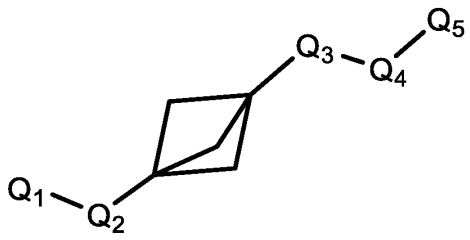
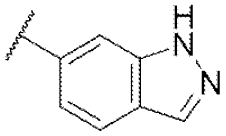
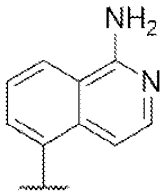
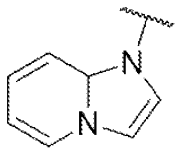
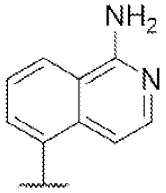
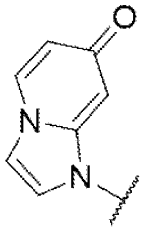
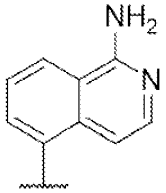
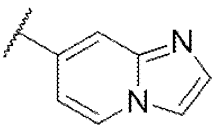
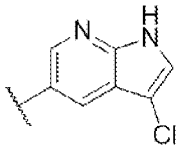
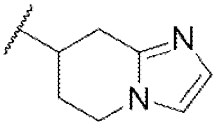
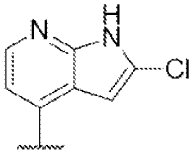
Example No	Q_1	Q_2	Q_3	Q_4	Q_5
1120		OCH_2	absent	NH	
1121		OCH_2	absent	NH	
1122		OCH_2	absent	NH	
1123		CH_2O	absent	NH	
1124		CH_2O	absent	NH	

Table 1b



Example No	Q_1	Q_2	Q_3	Q_4	Q_5
1125		OCH_2	CH_2	NH	
1126		CH_2	CH_2	NH	
1127		CH_2	CH_2	NH	
1129		OCH_2	CH_2	NH	
1130		OCH_2	CH_2	NH	

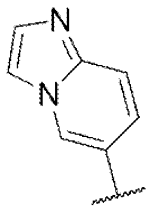
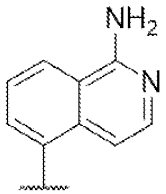
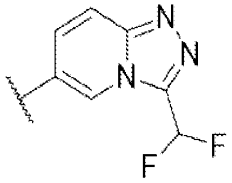
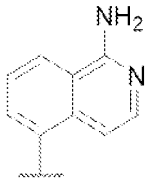
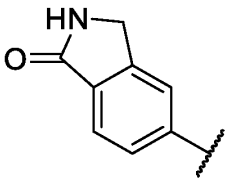
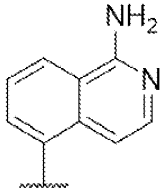
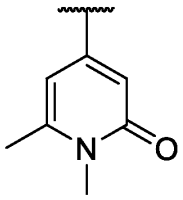
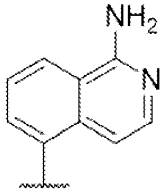
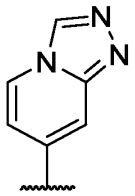
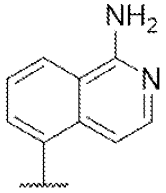
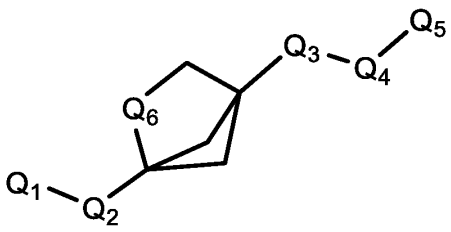
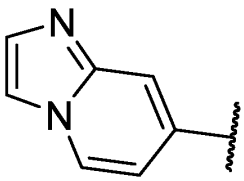
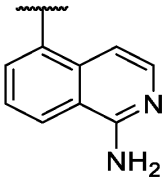
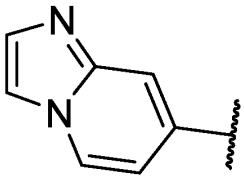
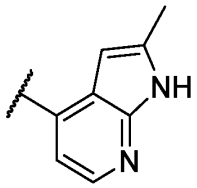
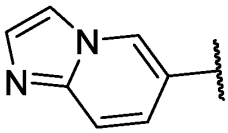
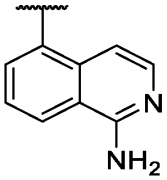
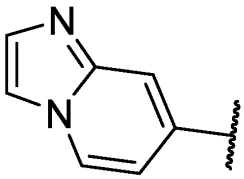
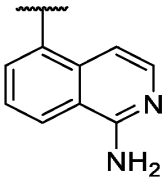
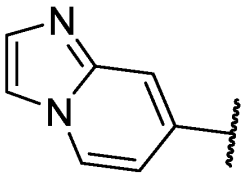
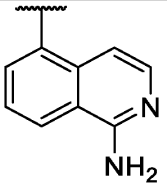
Example No	Q_1	Q_2	Q_3	Q_4	Q_5
1131		OCH_2	Absent	NH	
1132		CONH	CH_2	NH	
1133		OCH_2	CH2	NH	
1134		OCH_2	CH_2	NH	
1135		OCH_2	CH_2	NH	

Table 2a



Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
2020		OCH_2	CH_2	NH		O
2021		OCH_2	CH_2	NH		O
2022		OCH_2	CH_2	NH		O
2201		OCH_2	CH_2	O		NH
2202		OCH_2	CH_2	O		$NCOCH_3$

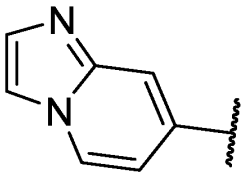
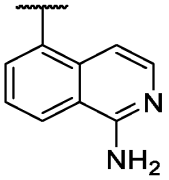
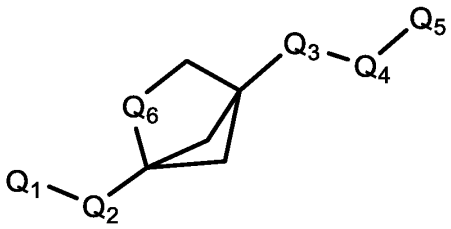
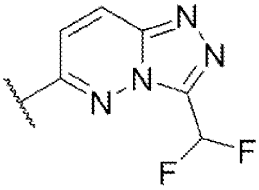
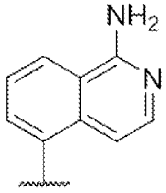
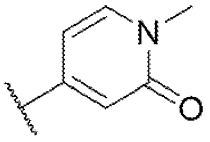
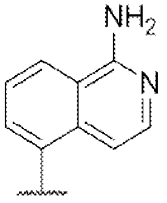
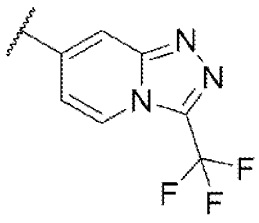
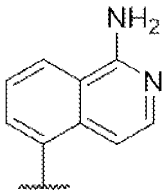
Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
2203		OCH_2	CH_2	O		CH_2

Table 2b



Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
2204		OCH_2	CH_2	NH		O
2205		OCH_2	CH_2	NH		O
2206		OCH_2	CH_2	NH		O

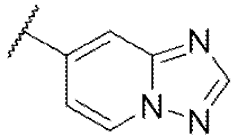
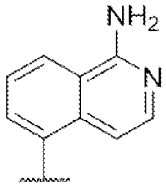
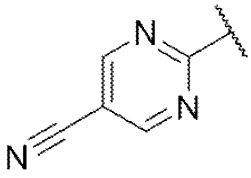
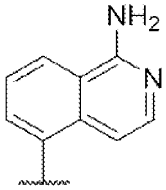
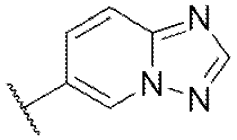
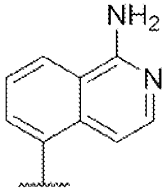
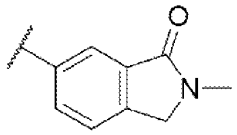
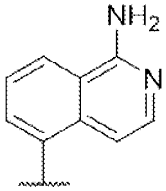
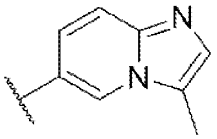
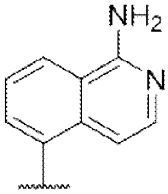
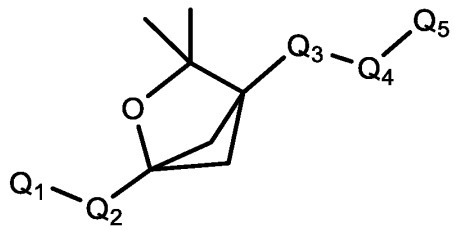
Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
2207		OCH_2	CH_2	NH		O
2208		OCH_2	CH_2	NH		O
2210		OCH_2	CH_2	NH		O
2211		OCH_2	CH_2	NH		O
2212		OCH_2	CH_2	NH		O

Table 3a



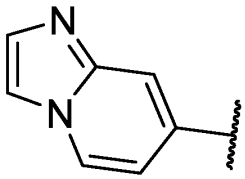
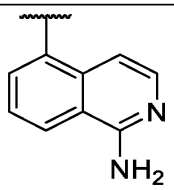
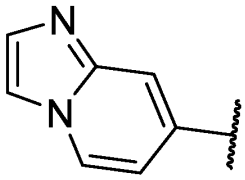
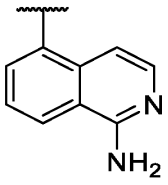
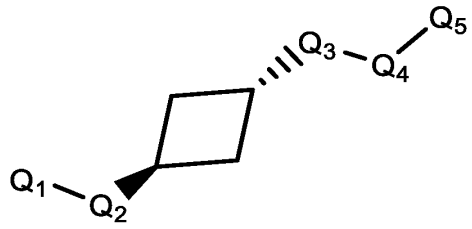
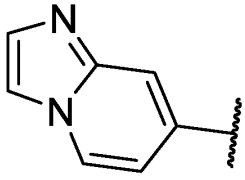
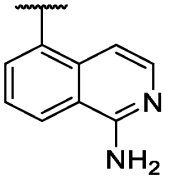
Example No	Q_1	Q_2	Q_3	Q_4	Q_5
3023		OCH_2	CH_2	NH	
3024		OCH_2	CH_2	O	

Table 4a



Example No	Q_1	Q_2	Q_3	Q_4	Q_5
4401		OCH_2	CH_2	NH	

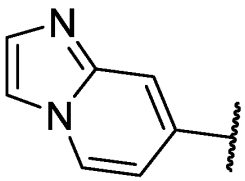
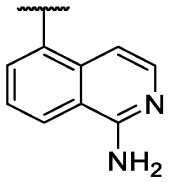
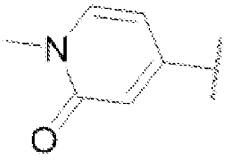
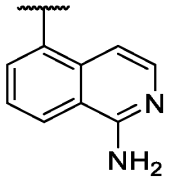
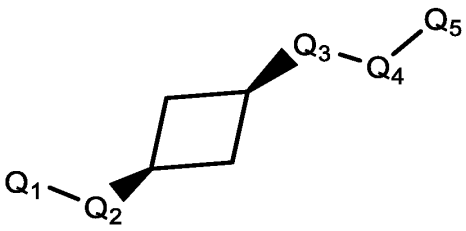
Example No	Q_1	Q_2	Q_3	Q_4	Q_5
4402		CH_2O	CH_2	NH	
4403		CH_2O	CH_2	NH	

Table 5b



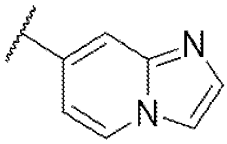
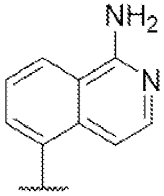
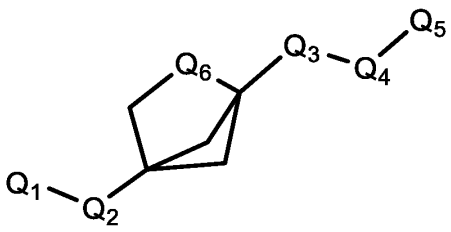
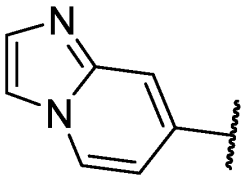
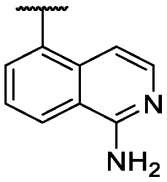
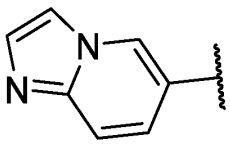
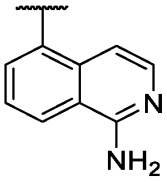
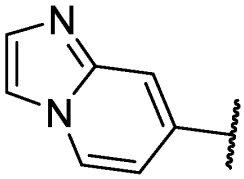
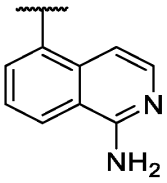
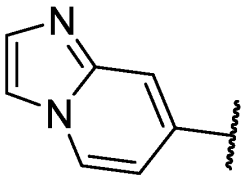
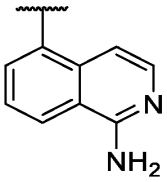
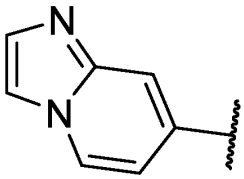
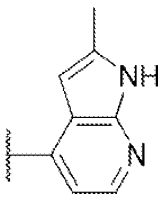
Example No	Q_1	Q_2	Q_3	Q_4	Q_5	
5003		OCH_2	CH_2	NH		242.7

Table 6a



Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
6601		OCH_2	CH_2	NH		O
6602		OCH_2	CH_2	NH		O
6603		OCH_2	CH_2	O		NH
6604		OCH_2	CH_2	O		$NCOCH_3$
6605		OCH_2	CH_2	NH		O

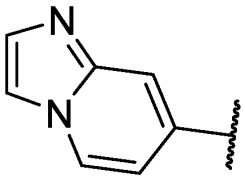
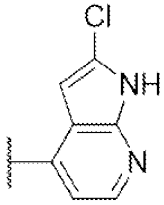
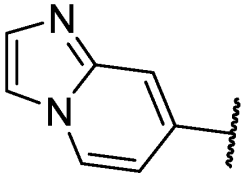
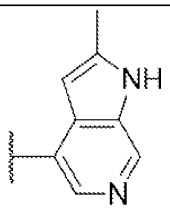
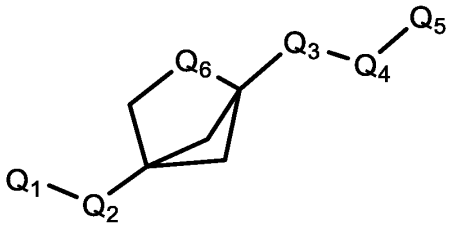
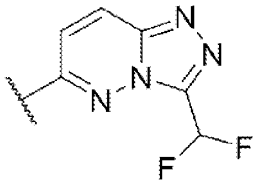
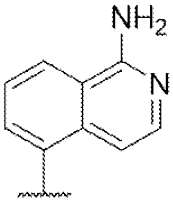
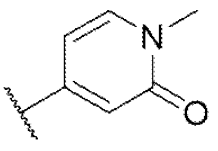
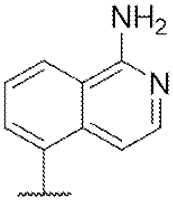
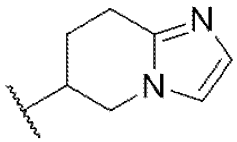
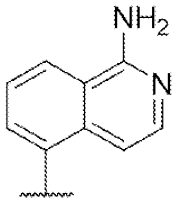
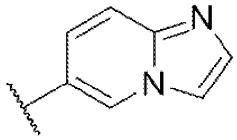
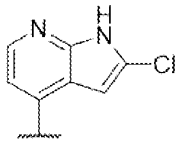
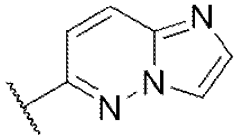
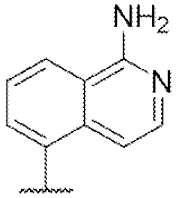
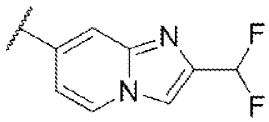
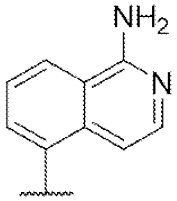
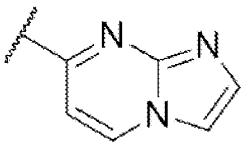
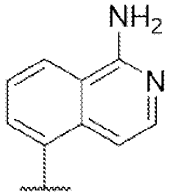
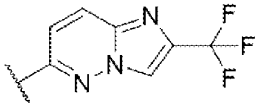
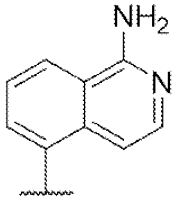
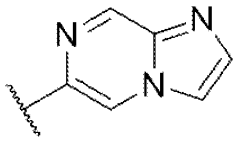
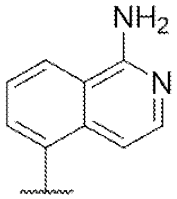
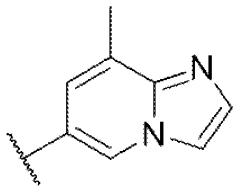
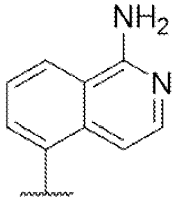
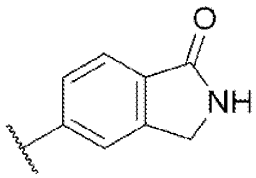
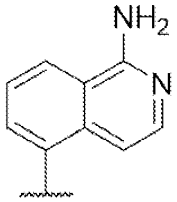
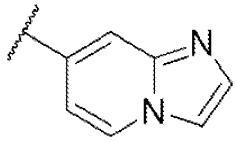
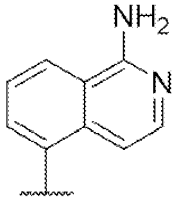
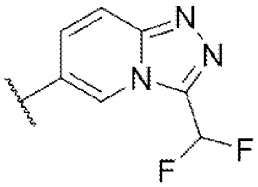
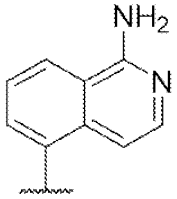
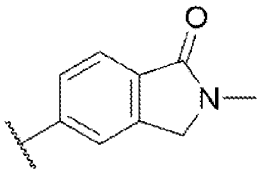
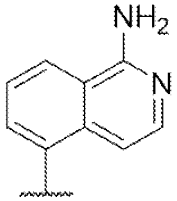
Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
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6607		OCH_2	CH_2	NH		O

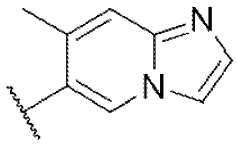
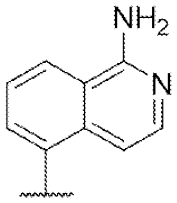
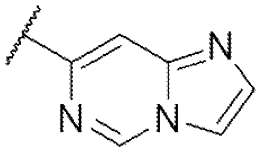
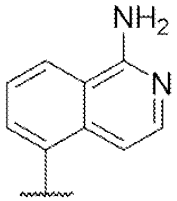
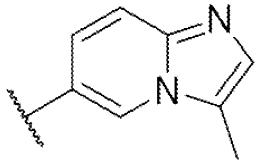
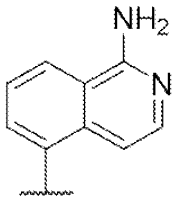
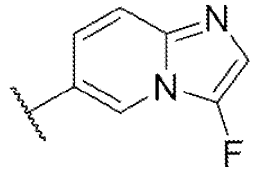
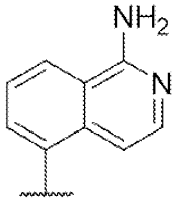
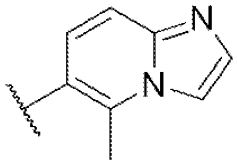
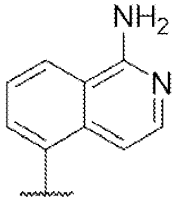
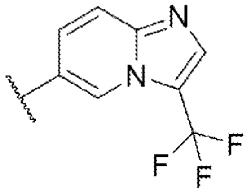
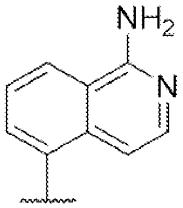
Table 6b

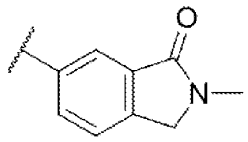
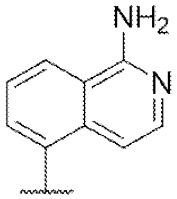
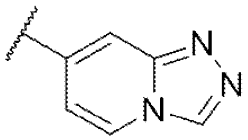
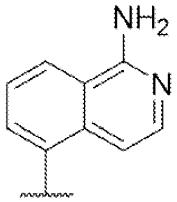
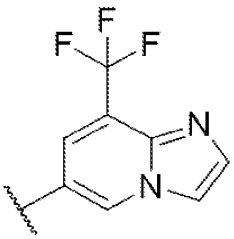
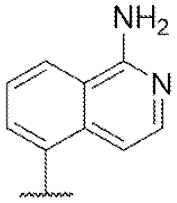
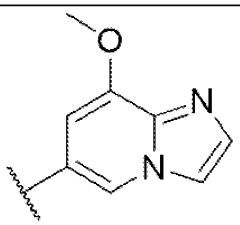
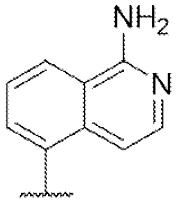
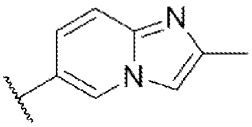
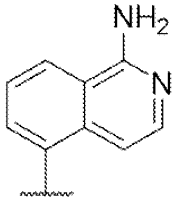
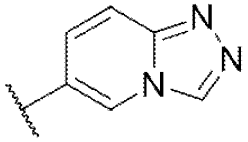
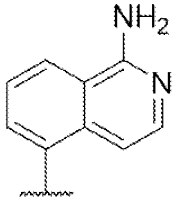


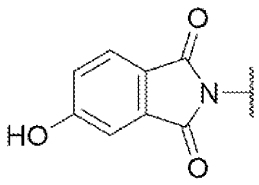
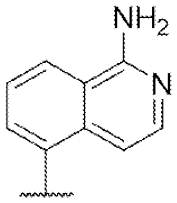
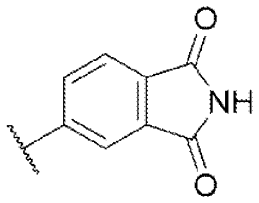
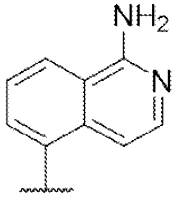
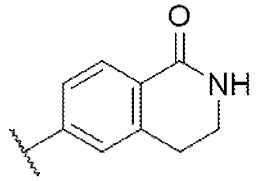
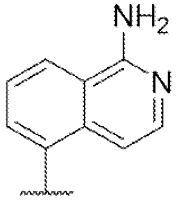
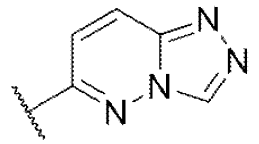
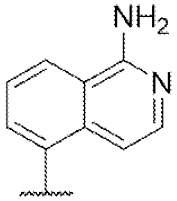
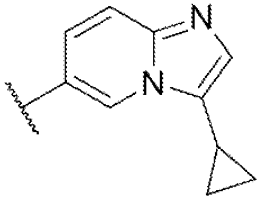
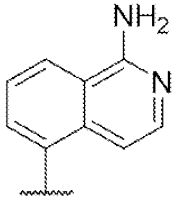
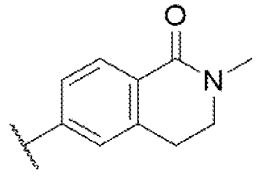
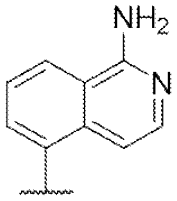
Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
6608		OCH_2	CH_2	NH		O
6609		OCH_2	CH_2	NH		O

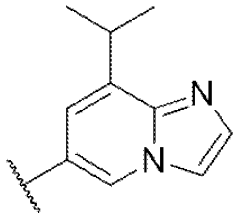
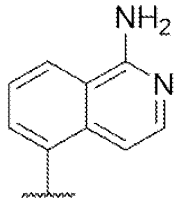
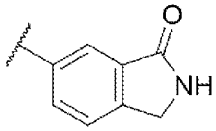
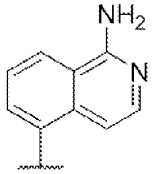
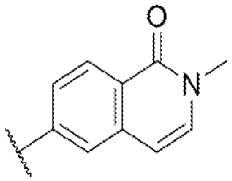
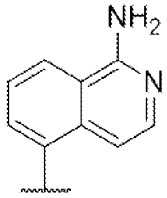
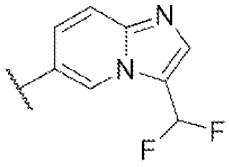
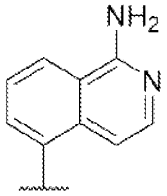
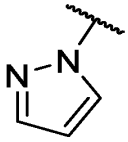
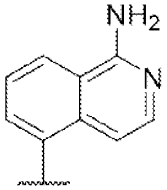
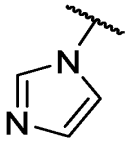
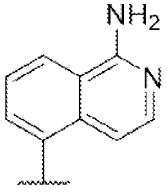
Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
6610		OCH_2	CH_2	NH		O
6611		OCH_2	CH_2	NH		O
6612		OCH_2	CH_2	NH		O
6613		OCH_2	CH_2	NH		O
6614		OCH_2	CH_2	NH		O
6615		OCH_2	CH_2	NH		O

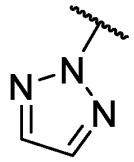
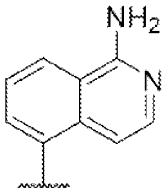
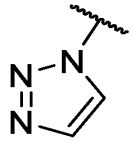
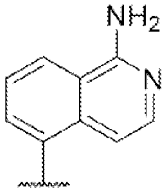
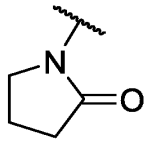
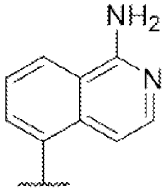
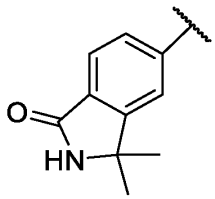
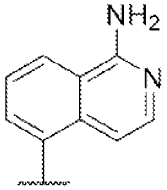
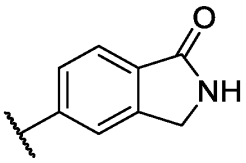
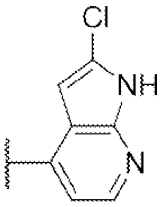
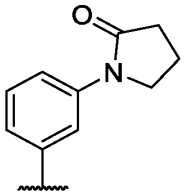
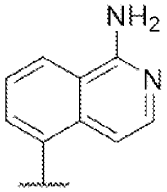
Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
6616		OCH_2	CH_2	NH		O
6617		OCH_2	CH_2	NH		O
6618		OCH_2	CH_2	NH		O
6619		$NHCH_2$	CH_2	O		O
6620		OCH_2	CH_2	NH		O
6621		OCH_2	CH_2	NH		O

Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
6622		OCH_2	CH_2	NH		O
6623		OCH_2	CH_2	NH		O
6624		OCH_2	CH_2	NH		O
6625		OCH_2	CH_2	NH		O
6626		OCH_2	CH_2	NH		O
6627		OCH_2	CH_2	NH		O

Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
6628		OCH_2	CH_2	NH		O
6629		OCH_2	CH_2	NH		O
6630		OCH_2	CH_2	NH		O
6631		OCH_2	CH_2	NH		O
6633		OCH_2	CH_2	NH		O
6634		OCH_2	CH_2	NH		O

Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
6635		CH_2	CH_2	NH		O
6636		OCH_2	CH_2	NH		O
6637		OCH_2	CH_2	NH		O
6638		OCH_2	CH_2	NH		O
6639		OCH_2	CH_2	NH		O
6640		OCH_2	CH_2	NH		O

Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
6641		OCH_2	CH_2	NH		O
6642		OCH_2	CH_2	NH		O
6643		OCH_2	CH_2	NH		O
6644		OCH_2	CH_2	NH		O
6645		CH2	CH_2	NH		O
6646		CH_2	CH_2	NH		O

Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
6647		CH_2	CH_2	NH		O
6648		CH_2	CH_2	NH		O
6649		CH_2	CH_2	NH		O
6650		OCH_2	CH_2	NH		O
6651		OCH_2	CH_2	NH		O
6653		OCH_2	CH_2	NH		O

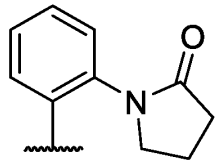
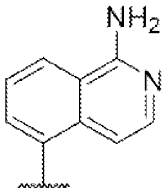
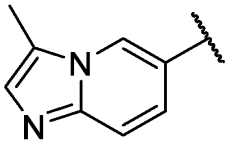
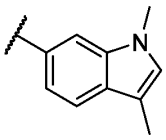
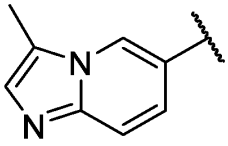
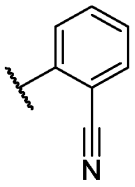
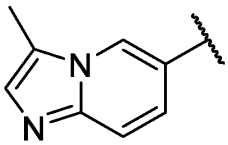
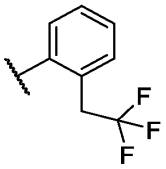
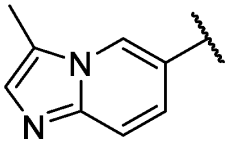
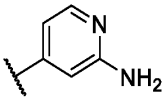
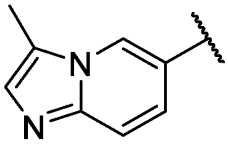
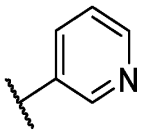
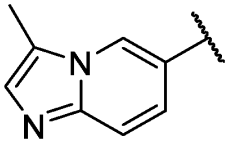
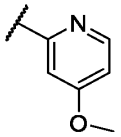
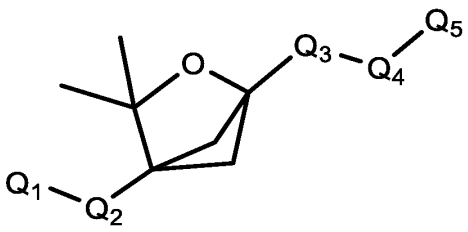
Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
6654		OCH_2	CH_2	NH		O
6656		OCH_2	CH_2	NH		O
6658		OCH_2	CH_2	NH		O
6659		OCH_2	CH_2	NH		O
6660		OCH_2	CH_2	NH		O
6661		OCH_2	CH_2	NH		O
6663		OCH_2	CH_2	NH		O

Table 7a



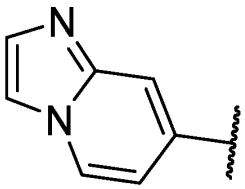
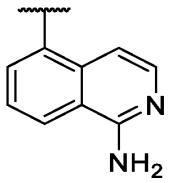
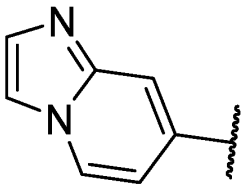
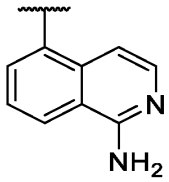
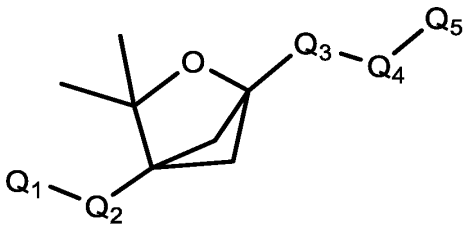
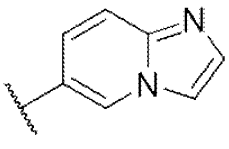
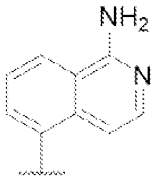
Example No	Q_1	Q_2	Q_3	Q_4	Q_5
7701		OCH_2	CH_2	NH	
7702		OCH_2	CH_2	O	

Table 7b



Example Number	Q_1	Q_2	Q_3	Q_4	Q_5
7703		OCH_2	CH_2	NH	

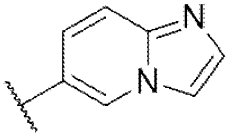
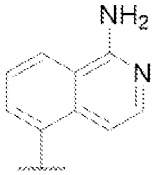
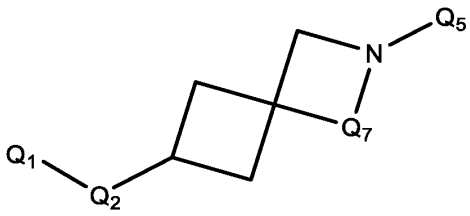
Example Number	Q_1	Q_2	Q_3	Q_4	Q_5
7704		OCH_2	CH_2	O	

Table 8a



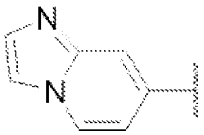
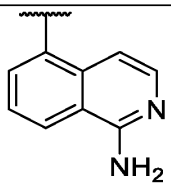
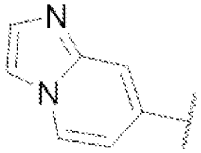
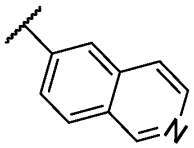
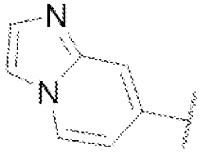
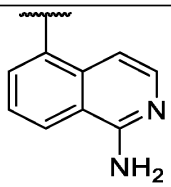
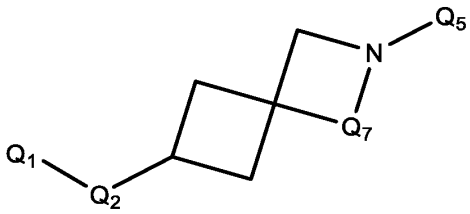
Example No	Q_1	Q_2	Q_5	Q_7
8801		CH_2O		CH_2
8802		CH_2O		CH_2
8803		CH_2O		CH_2CH_2

Table 8b



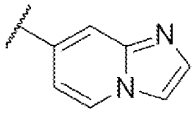
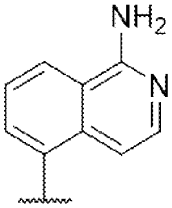
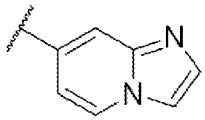
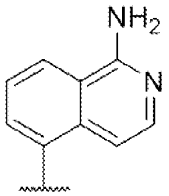
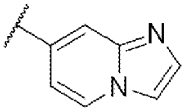
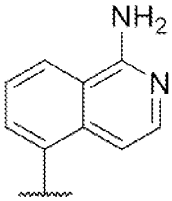
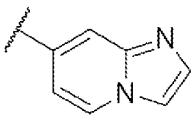
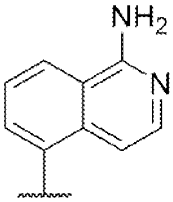
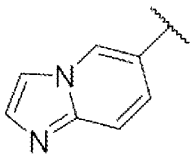
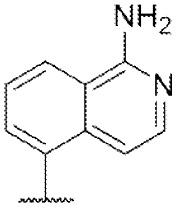
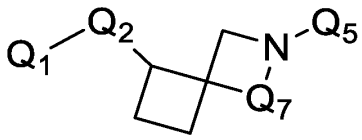
Example No	Q_1	Q_2	Q_5	Q_7
8804		CH_2O		CH_2CH_2
8805		CH_2O		CH_2CH_2
8806		OCH_2		CH_2CH_2
8807		OCH_2		CH_2CH_2
8808		OCH_2		CH_2

Table 9b



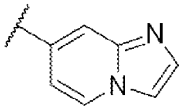
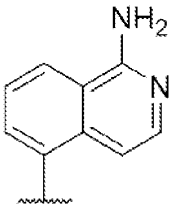
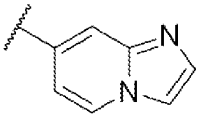
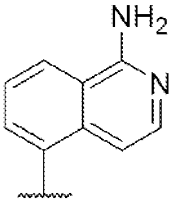
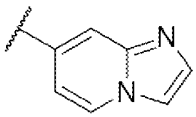
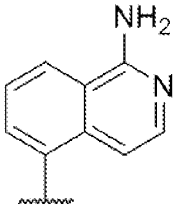
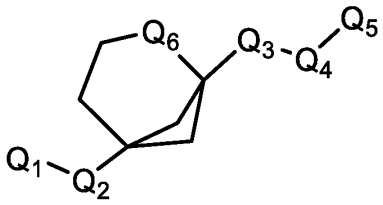
Example No	Q_1	Q_2	Q_5	Q_7
9001		CH_2O		CH_2
9002		CH_2O		CH_2
9003		CH_2O		CH_2

Table 10a



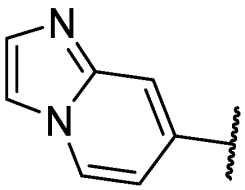
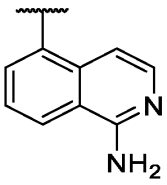
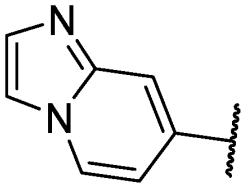
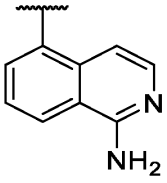
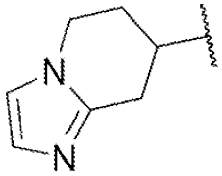
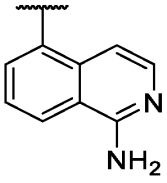
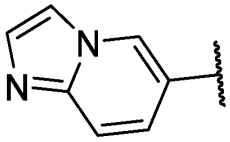
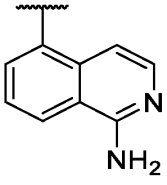
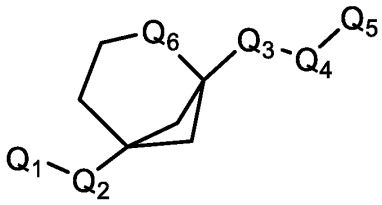
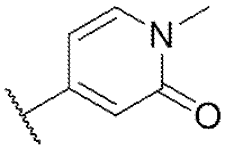
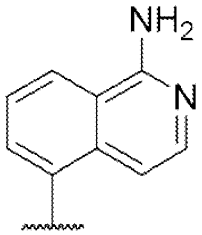
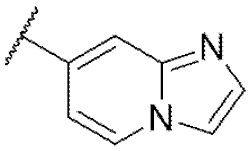
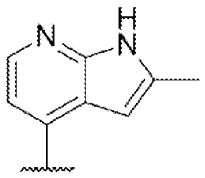
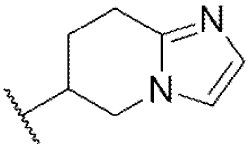
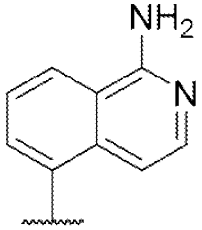
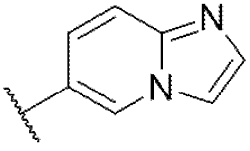
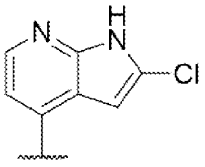
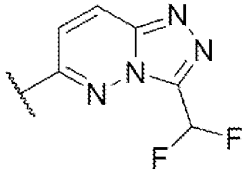
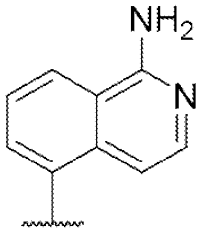
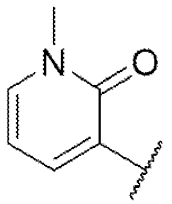
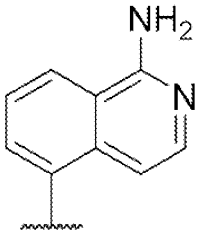
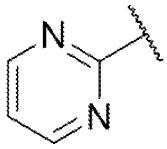
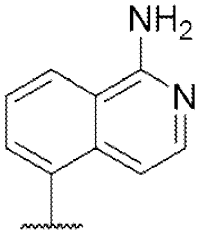
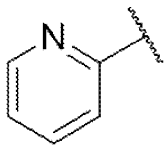
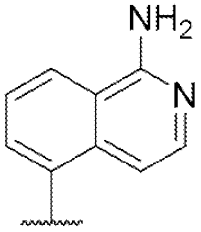
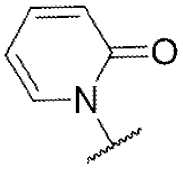
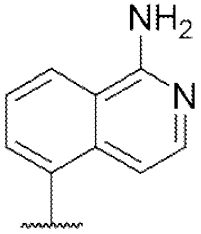
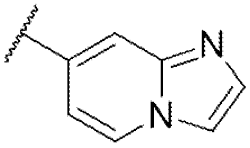
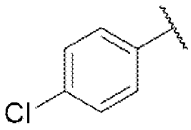
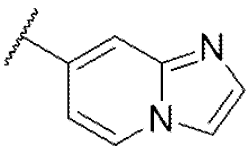
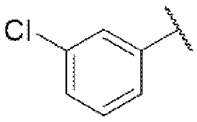
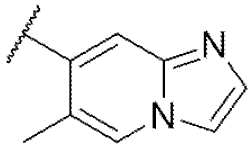
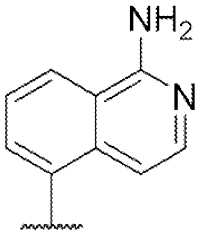
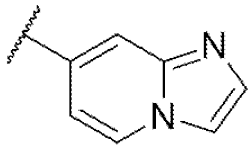
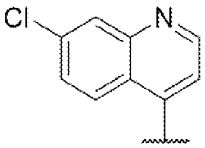
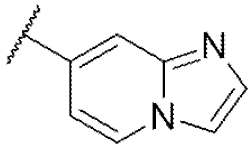
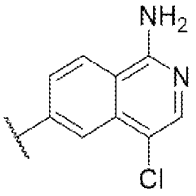
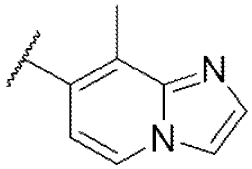
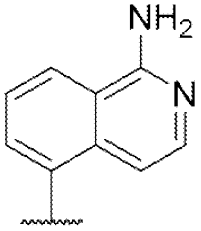
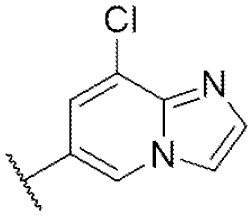
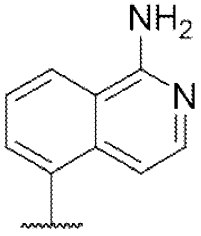
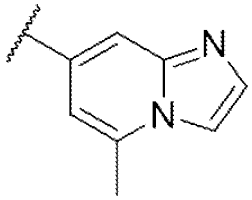
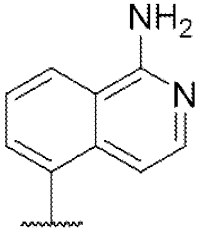
Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
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10904		OCH_2	CH_2	NH		O

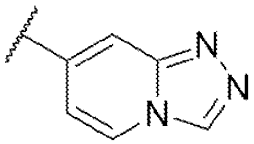
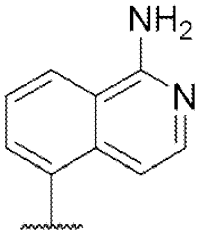
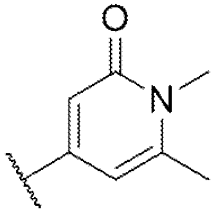
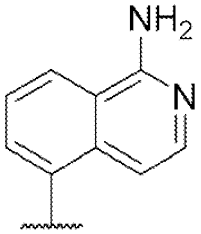
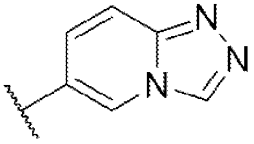
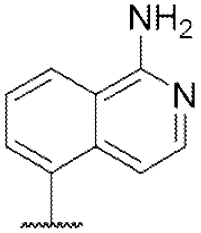
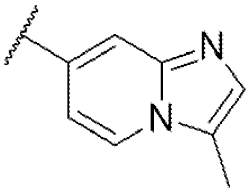
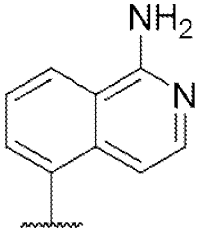
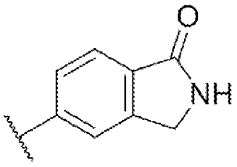
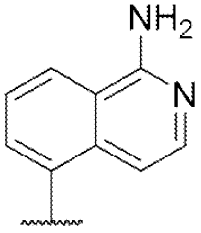
Table 10b

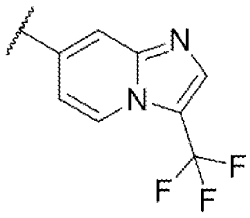
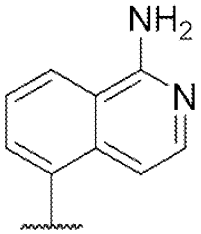
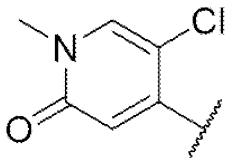
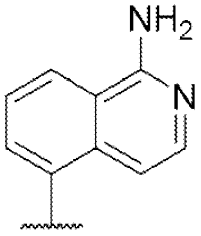
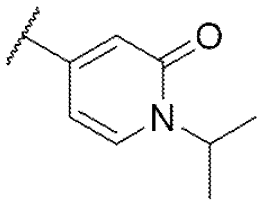
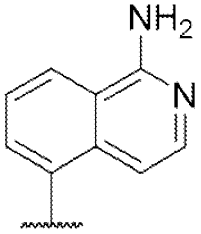
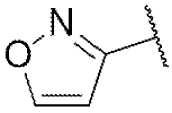
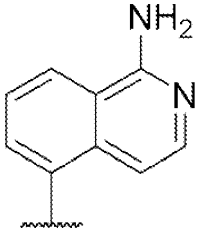
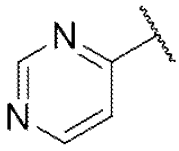
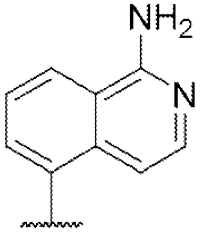


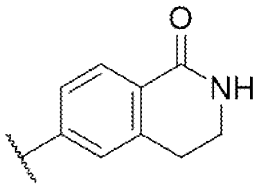
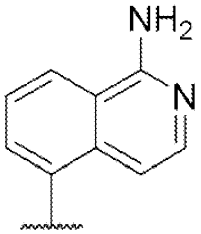
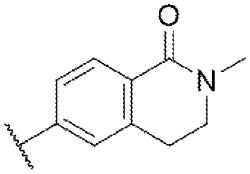
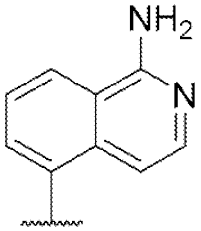
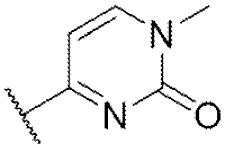
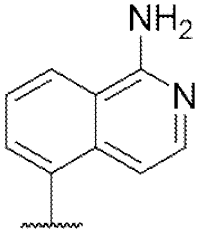
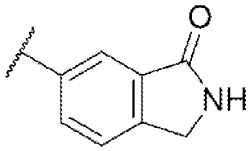
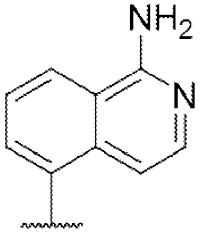
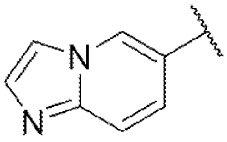
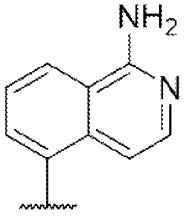
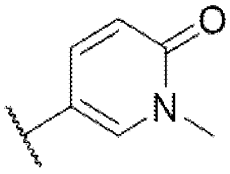
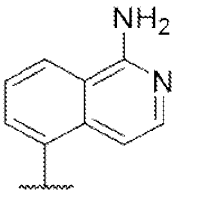
Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
10906		OCH_2	CH_2	NH		O
10907		OCH_2	CH_2	NH		O
10908		OCH_2	CH_2	NH		O
10909		OCH_2	CH_2	NH		O
10910		OCH_2	CH_2	NH		O

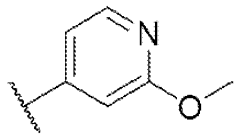
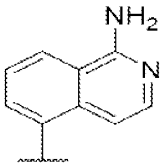
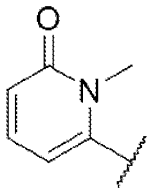
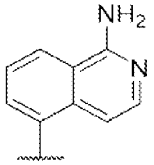
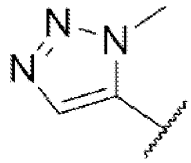
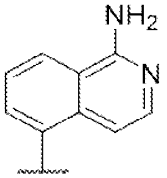
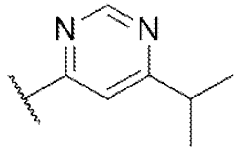
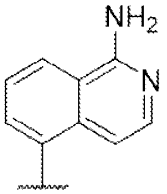
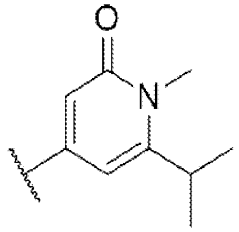
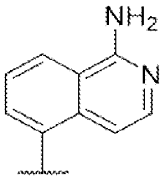
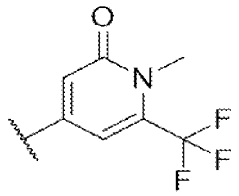
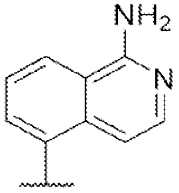
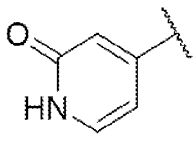
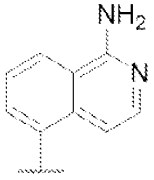
Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
10911		OCH_2	CH_2	NH		O
10912		OCH_2	CH_2	NH		O
10914		OCH_2	CH_2	NH		O
10915		CH_2	CH_2	NH		O
10918		OCH_2	CH_2	NH		O
10919		OCH_2	CH_2	NH		O

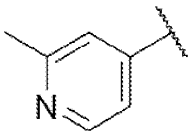
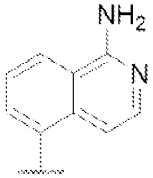
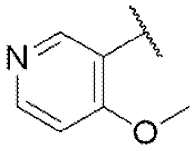
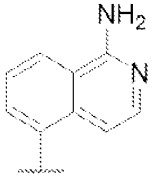
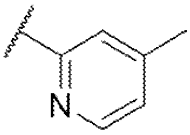
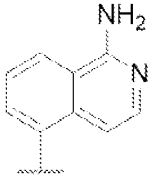
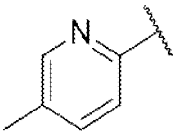
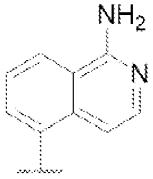
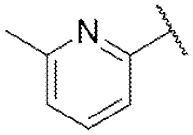
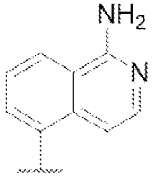
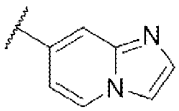
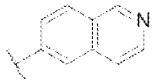
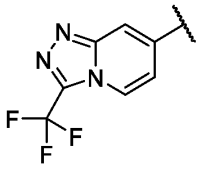
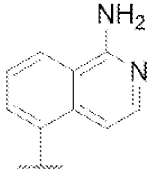
Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
10920		OCH_2	CH_2	NH		O
10921		OCH_2	CH_2	NH		O
10922		OCH_2	CH_2	NH		O
10923		OCH_2	CH_2	NH		O
10924		OCH_2	CH_2	NH		O
10925		OCH_2	CH_2	NH		O

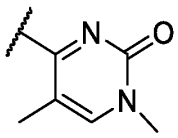
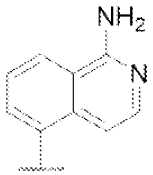
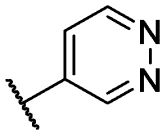
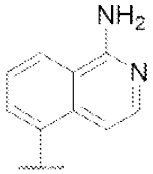
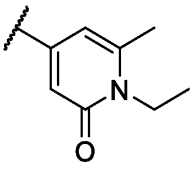
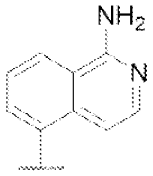
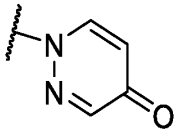
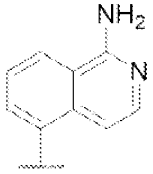
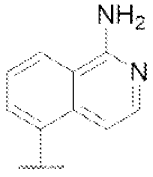
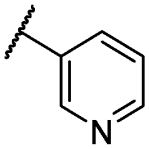
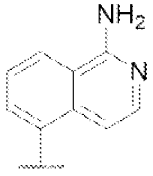
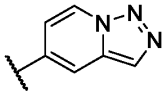
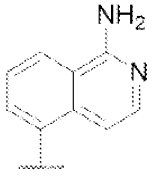
Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
10926		OCH_2	CH_2	NH		O
10928		OCH_2	CH_2	NH		O
10929		OCH_2	CH_2	NH		O
10930		OCH_2	CH_2	NH		O
10931		OCH_2	CH_2	NH		O

Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
10932		OCH_2	CH_2	NH		O
10933		OCH_2	CH_2	NH		O
10934		OCH_2	CH_2	NH		O
10936		OCH_2	CH_2	NH		O
10937		OCH_2	CH_2	NH		O

Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
10938		OCH_2	CH_2	NH		O
10939		OCH_2	CH_2	NH		O
10940		OCH_2	CH_2	NH		O
10941		OCH_2	CH_2	NH		O
10942		OCH_2	CH_2	NH		CH2
10943		OCH_2	CH_2	NH		O

Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
10944		OCH_2	CH_2	NH		O
10945		OCH_2	CH_2	NH		O
10946		OCH_2	CH_2	NH		O
10948		OCH_2	CH_2	NH		O
10949		OCH_2	CH_2	NH		O
10951		OCH_2	CH_2	NH		O
10952		OCH_2	CH_2	NH		O

Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
10953		OCH_2	CH_2	NH		O
10954		OCH_2	CH_2	NH		O
10955		OCH_2	CH_2	NH		O
10956		OCH_2	CH_2	NH		O
10957		OCH_2	CH_2	NH		O
10958		OCH_2	CH_2	NH		O
10961		OCH_2	CH_2	NH		O

Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
10962		OCH_2	CH_2	NH		O
10963		OCH_2	CH_2	NH		O
10964		OCH_2	CH_2	NH		O
10965		CH_2	CH_2	NH		O
10966		CH_2	CH_2	NH		O
10968		OCH_2	CH_2	NH		O
10969		OCH_2	CH_2	NH		O

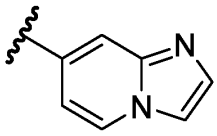
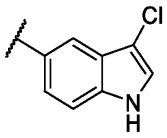
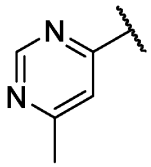
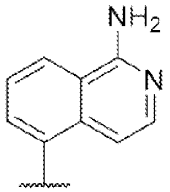
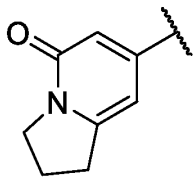
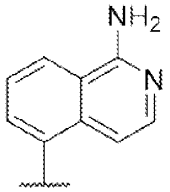
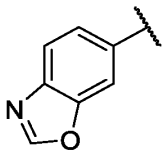
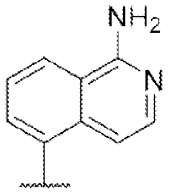
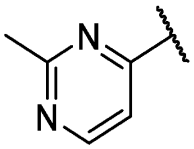
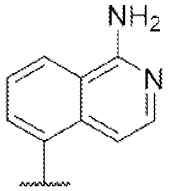
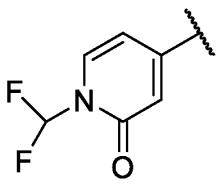
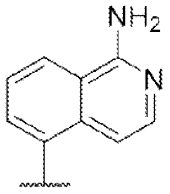
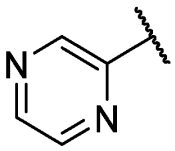
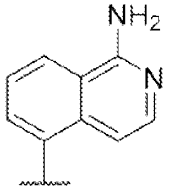
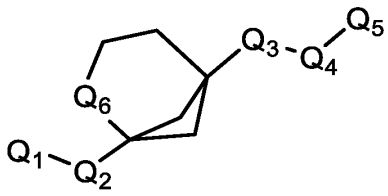
Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
10970		OCH_2	CH_2	NH		O
10971		OCH_2	CH_2	NH		O
10972		OCH_2	CH_2	NH		O
10973		OCH_2	CH_2	NH		O
10974		OCH_2	CH_2	NH		O
10975		OCH_2	CH_2	NH		O
10976		OCH_2	CH_2	NH		O

Table 11b



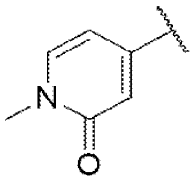
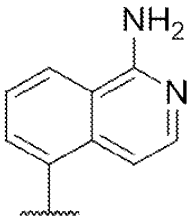
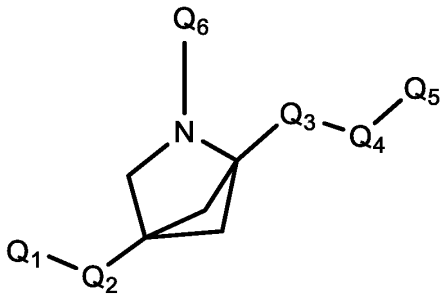
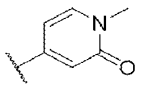
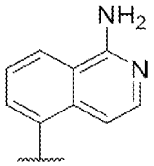
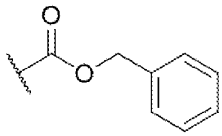
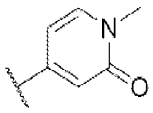
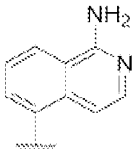
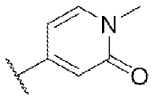
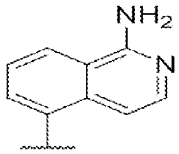
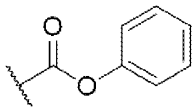
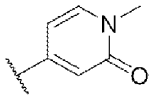
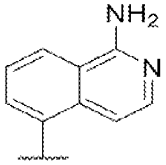
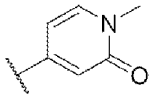
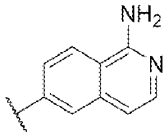
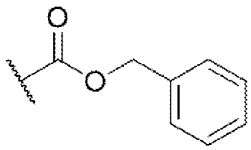
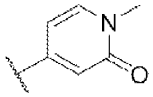
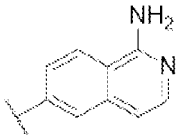
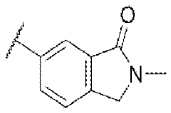
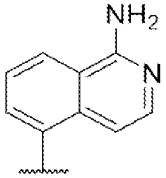
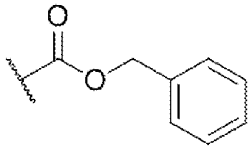
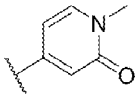
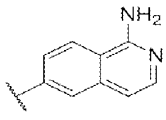
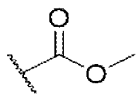
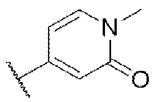
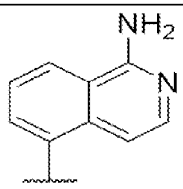
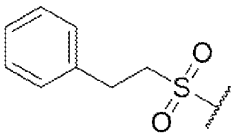
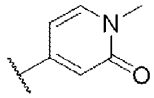
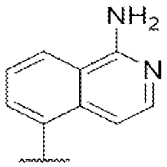
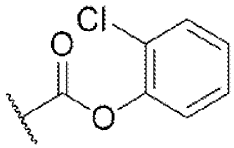
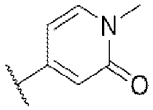
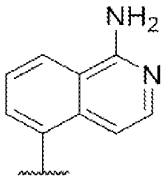
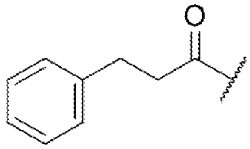
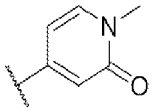
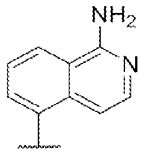
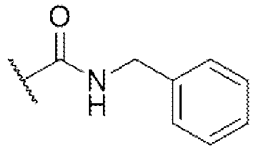
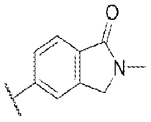
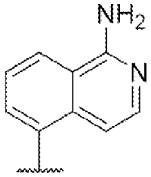
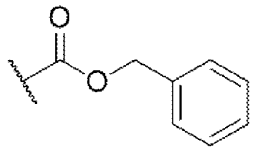
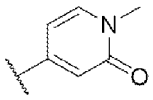
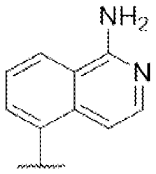
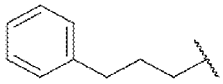
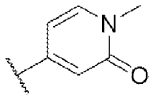
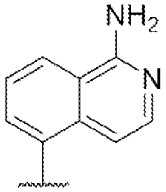
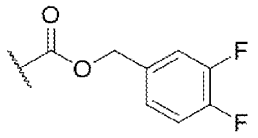
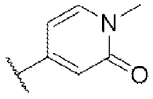
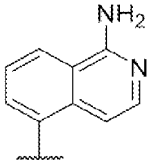
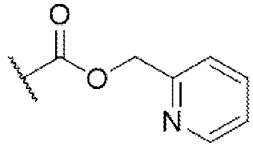
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11001		OCH_2	CH_2	NH		O

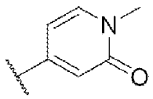
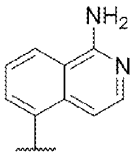
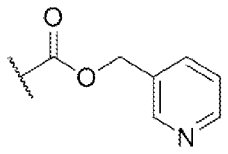
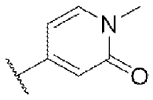
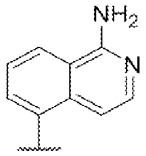
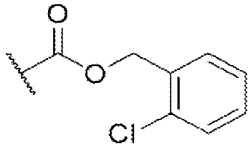
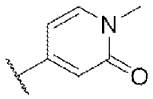
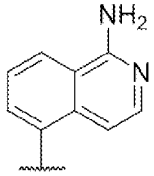
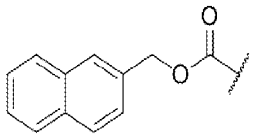
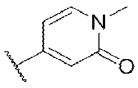
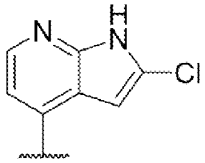
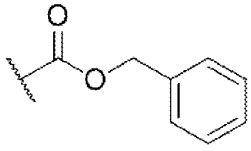
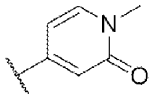
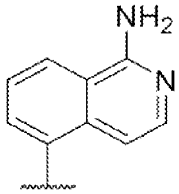
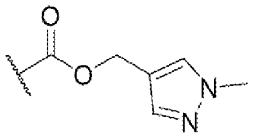
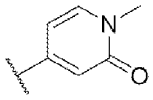
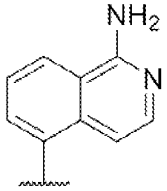
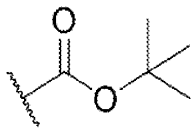
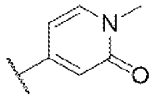
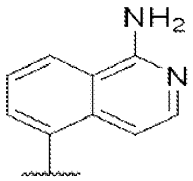
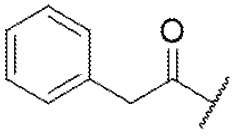
Table 12b

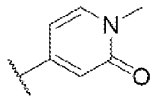
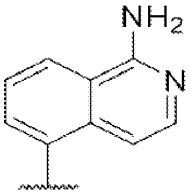
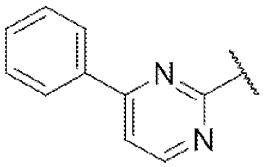
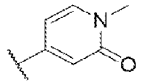
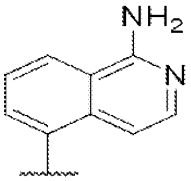
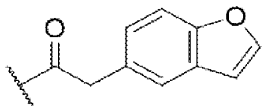
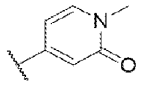
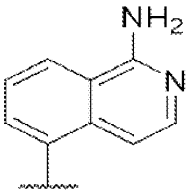
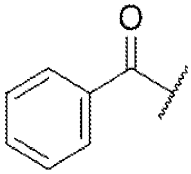
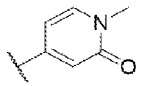
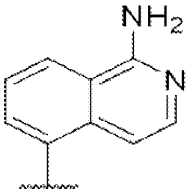
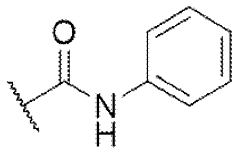
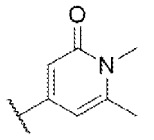
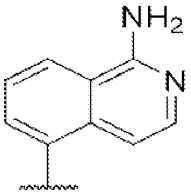
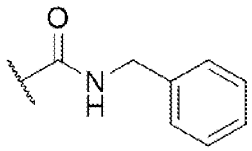
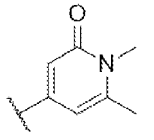
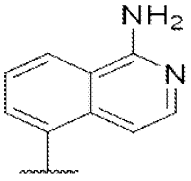
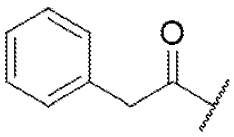


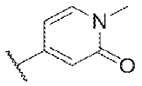
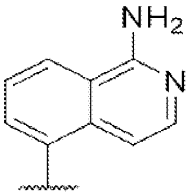
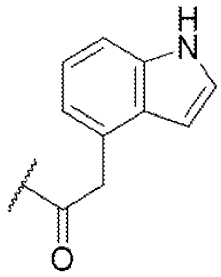
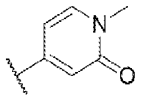
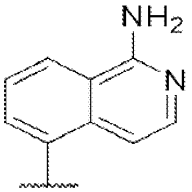
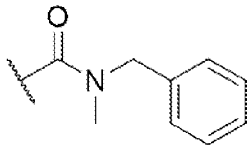
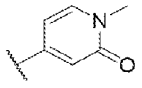
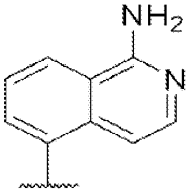
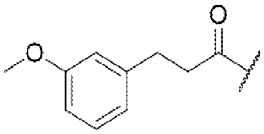
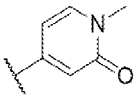
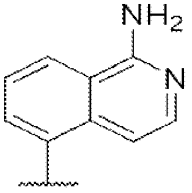
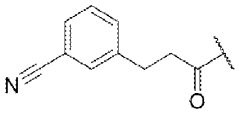
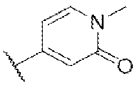
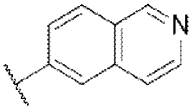
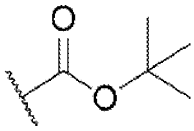
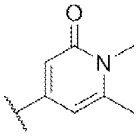
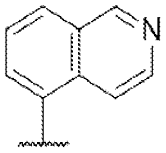
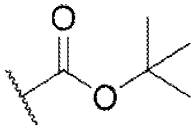
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12001		OCH_2	CH_2	NH		

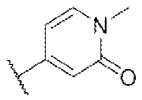
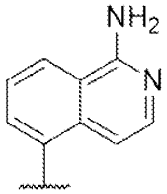
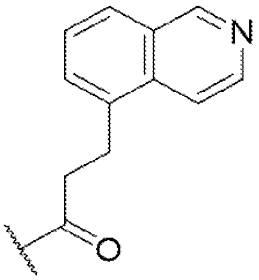
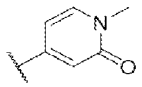
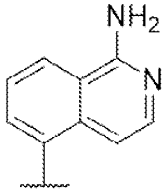
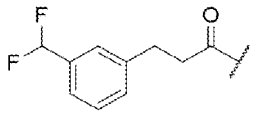
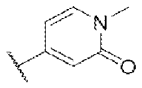
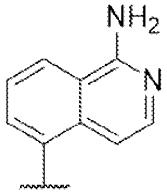
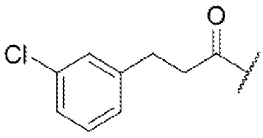
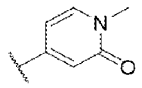
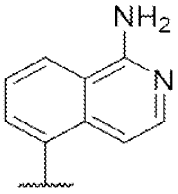
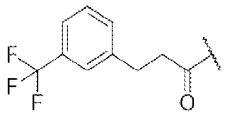
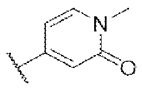
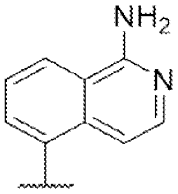
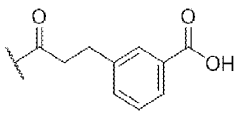
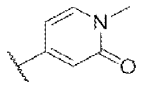
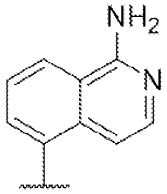
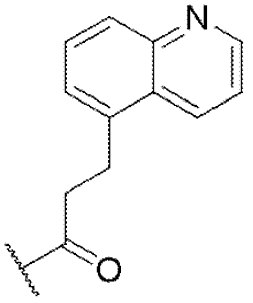
Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
12007		OCH_2	CH_2	NH		H
12008		OCH_2	CH_2	NH		
12009		OCH_2	CH_2	NH		
12010		OCH_2	CH_2	NH		
12011		OCH_2	CH_2	NH		H
12012		OCH_2	CH_2	NH		
12013		OCH_2	CH_2	NH		
12014		OCH_2	CH_2	NH		

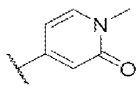
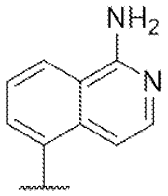
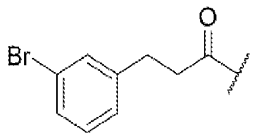
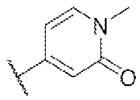
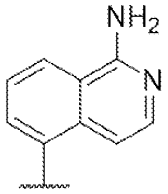
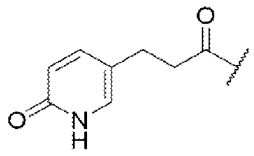
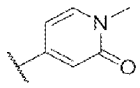
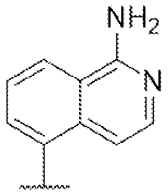
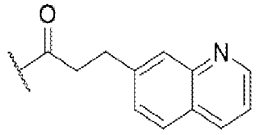
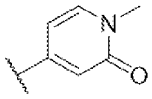
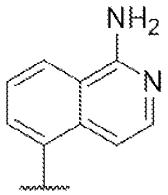
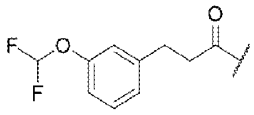
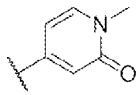
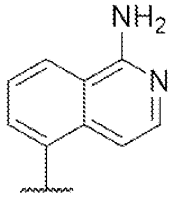
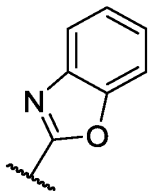
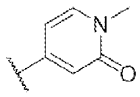
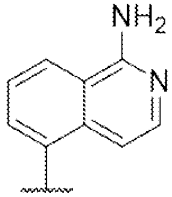
Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
12015		OCH_2	CH_2	NH		
12016		OCH_2	CH_2	NH		
12017		OCH_2	CH_2	NH		
12018		OCH_2	CH_2	NH		
12019		OCH_2	CH_2	NH		
12020		OCH_2	CH_2	NH		
12021		OCH_2	CH_2	NH		

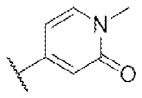
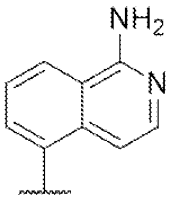
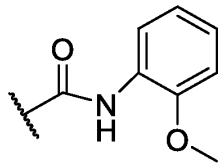
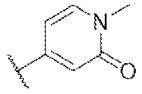
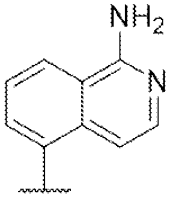
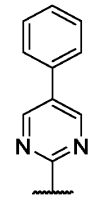
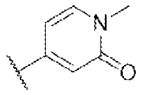
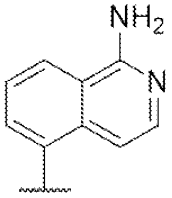
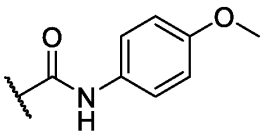
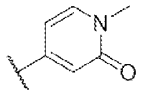
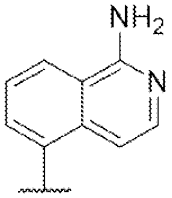
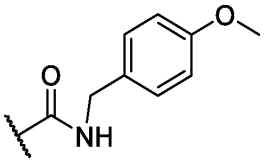
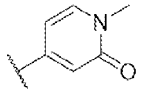
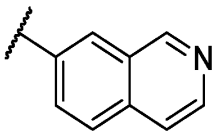
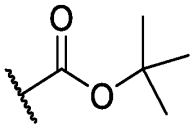
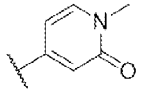
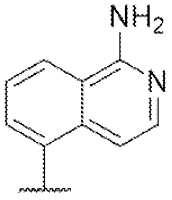
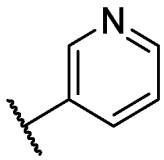
Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
12022		OCH_2	CH_2	NH		
12023		OCH_2	CH_2	NH		
12024		OCH_2	CH_2	NH		
12025		OCH_2	CH_2	NH		
12026		OCH_2	CH_2	NH		
12027		OCH_2	CH_2	NH		
12028		OCH_2	CH_2	NH		

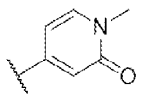
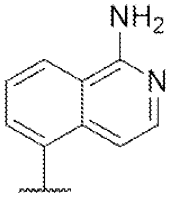
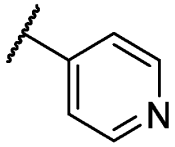
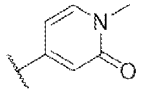
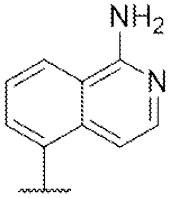
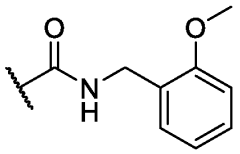
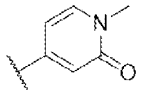
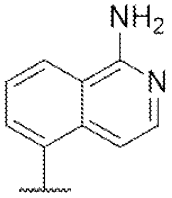
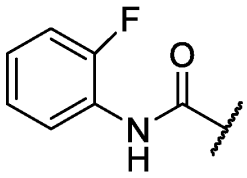
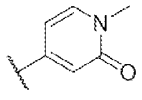
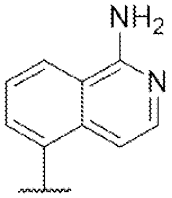
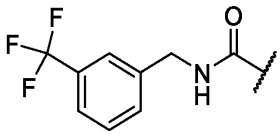
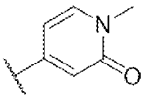
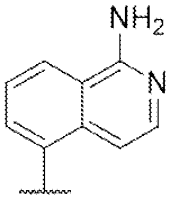
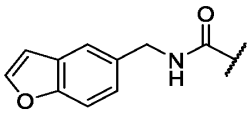
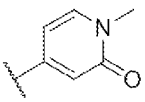
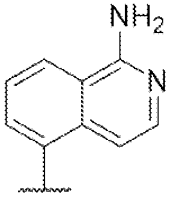
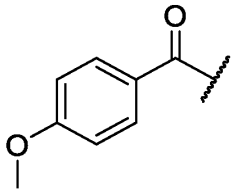
Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
12031		OCH_2	CH_2	NH		
12034		OCH_2	CH_2	NH		
12035		OCH_2	CH_2	NH		
12036		OCH_2	CH_2	NH		
12038		OCH_2	CH_2	NH		
12039		OCH_2	CH_2	NH		

Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
12040		OCH_2	CH_2	NH		
12041		OCH_2	CH_2	NH		
12042		OCH_2	CH_2	NH		
12044		OCH_2	CH_2	NH		
12045		OCH_2	CH_2	NH		
12046		OCH_2	CH_2	NH		

Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
12047		OCH_2	CH_2	NH		
12048		OCH_2	CH_2	NH		
12049		OCH_2	CH_2	NH		
12050		OCH_2	CH_2	NH		
12051		OCH_2	CH_2	NH		
12052		OCH_2	CH_2	NH		

Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
12053		OCH_2	CH_2	NH		
12054		OCH_2	CH_2	NH		
12055		OCH_2	CH_2	NH		
12056		OCH_2	CH_2	NH		
12057		OCH_2	CH_2	NH		
12058		OCH_2	CH_2	NH		

Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
12059		OCH_2	CH_2	NH		
12060		OCH_2	CH_2	NH		
12061		OCH_2	CH_2	NH		
12062		OCH_2	CH_2	NH		
12063		OCH_2	CH_2	NH		
12064		OCH_2	CH_2	NH		

Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
12065		OCH_2	CH_2	NH		
12067		OCH_2	CH_2	NH		
12068		OCH_2	CH_2	NH		
12069		OCH_2	CH_2	NH		
12070		OCH_2	CH_2	NH		
12071		OCH_2	CH_2	NH		

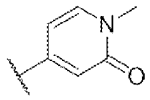
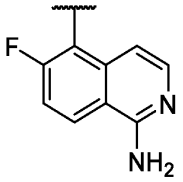
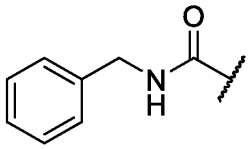
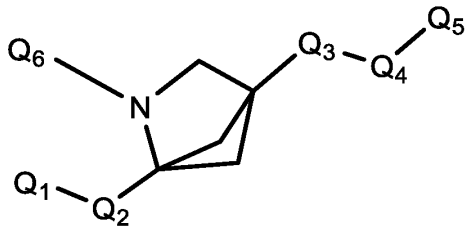
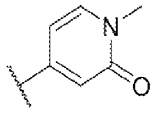
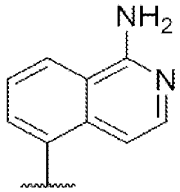
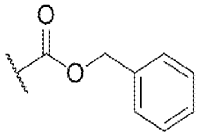
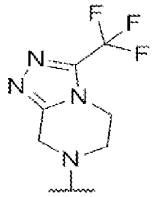
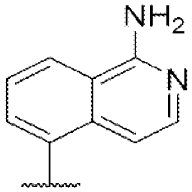
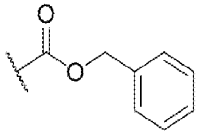
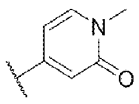
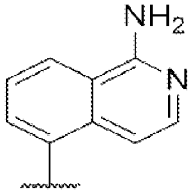
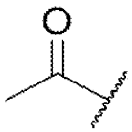
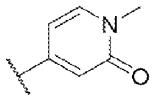
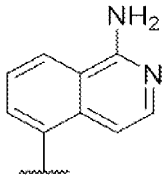
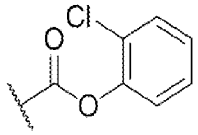
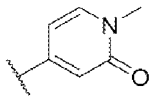
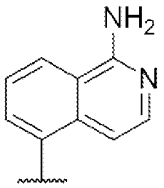
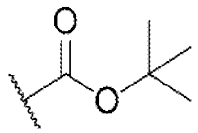
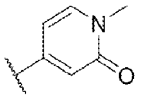
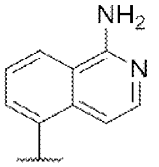
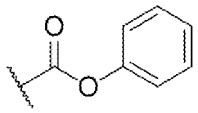
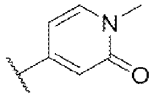
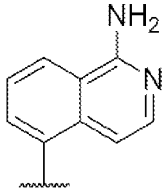
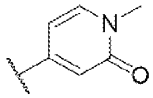
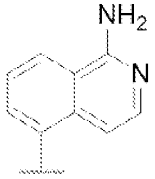
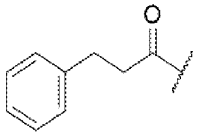
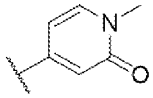
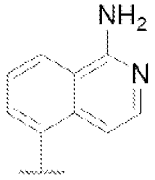
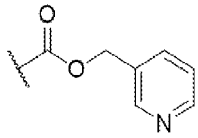
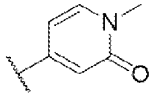
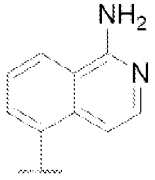
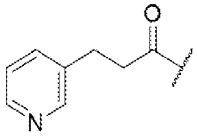
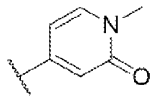
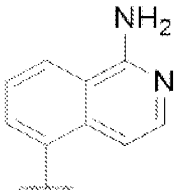
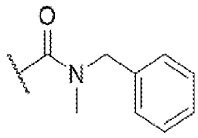
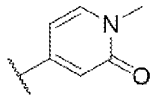
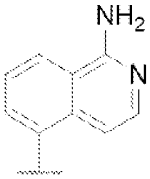
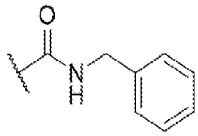
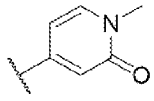
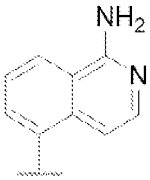
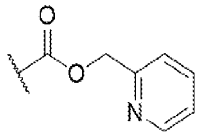
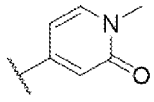
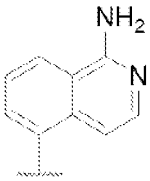
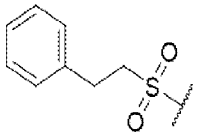
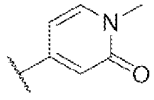
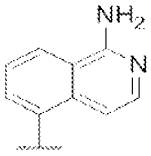
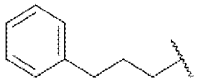
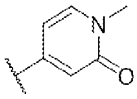
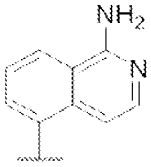
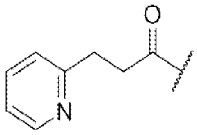
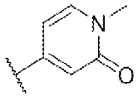
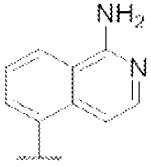
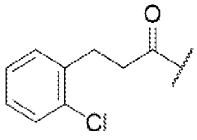
Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
12072		OCH_2	CH_2	NH		

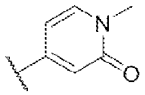
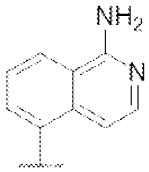
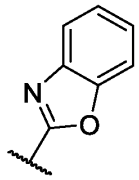
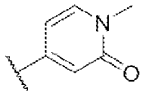
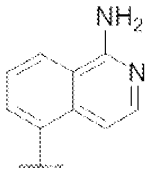
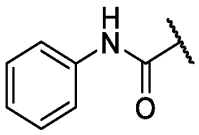
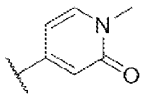
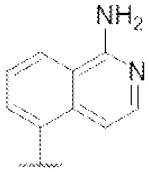
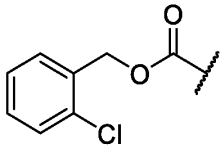
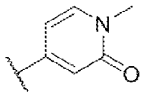
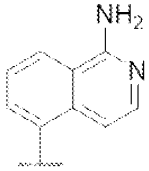
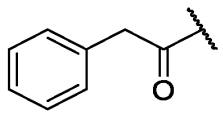
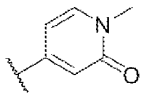
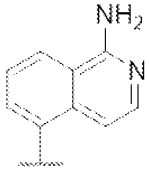
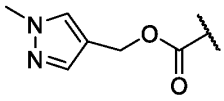
Table 13b



Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
13001		OCH_2	CH_2	NH		
13002		C=O	CH_2	NH		
13003		OCH_2	CH_2	NH		

Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
13004		OCH_2	CH_2	NH		
13005		OCH_2	CH_2	NH		
13006		OCH_2	CH_2	NH		
13007		OCH_2	CH_2	NH		H
13008		OCH_2	CH_2	NH		
13009		OCH_2	CH_2	NH		
13010		OCH_2	CH_2	NH		

Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
13011		OCH_2	CH_2	NH		
13012		OCH_2	CH_2	NH		
13013		OCH_2	CH_2	NH		
13014		OCH_2	CH_2	NH		
13015		OCH_2	CH_2	NH		
13016		OCH_2	CH_2	NH		
13017		OCH_2	CH_2	NH		

Example No	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6
13018		OCH_2	CH_2	NH		
13019		OCH_2	CH_2	NH		
13020		OCH_2	CH_2	NH		
13021		OCH_2	CH_2	NH		
13022		OCH_2	CH_2	NH		

Preferably, the compound of formula (I) is a compound selected from example numbers: 1001, 1002, 1002.1, 1002.2, 1004, 1005.1, 1006, 1009, 1010, 1011, 1012, 1013, 1014, 1015, 1016, 1017, 1018, 1019, 1101, 1105, 1109, 1110, 1113, 1118, 1125, 1126, 1127, 1129, 1130, 1131, 1132, 1133, 1134, 1135, 2020, 2022, 2204, 2205, 2206, 2207, 2208, 2210, 2211, 2212, 4401, 5003, 6601, 6602, 6605, 6606, 6608, 6609, 6610, 6611, 6612, 6613, 6614, 6615, 6616, 6617, 6618, 6619, 6620, 6621, 6622, 6623, 6624, 6625, 6626, 6627, 6628, 6629, 6630, 6631, 6633, 6634, 6635, 6636, 6637, 6638, 6639, 6640, 6641, 6642, 6643, 6644, 6645, 6646, 6647, 6648, 6649, 6650, 6651, 6653, 6654, 6656, 6658, 6659, 6660, 6661, 6663, 7702, 7703, 7704, 8801, 8803, 8804, 8805, 8806, 8807, 8808, 9001, 9002, 9003, 10901, 10903, 10904, 10906, 10907, 10908, 10909, 10910, 10911, 10912, 10914, 10915, 10918, 10919, 10920, 10921, 10922, 10923, 10924, 10925, 10926, 10928, 10929, 10930, 10931, 10932, 10933, 10934, 10936, 10937, 10938, 10939, 10940, 10941, 10942, 10943, 10944, 10945, 10946, 10948, 10949, 10951, 10952, 10953, 10954, 10955, 10956, 10957, 10958, 10961, 10962, 10963, 10964, 10965, 10966, 10968, 10969, 10970, 10971, 10972, 10973, 10974, 10975, 10976, 11001, 12001, 12007, 12008, 12009, 12010, 12011, 12012, 12013, 12014, 12015, 12016, 12017, 12018, 12019, 12020, 12021, 12022, 12023, 12024, 12025, 12026, 12027, 12028, 12031, 12034, 12035, 12036, 12038, 12039, 12040, 12041, 12042, 12044, 12045, 12046, 12047, 12048, 12049, 12050, 12051, 12052, 12053, 12054, 12055, 12056, 12057, 12058, 12059, 12060, 12061, 12062, 12063, 12064, 12065, 12067, 12068, 12069, 12070, 12071, 12072, 13001, 13002, 13003, 13004, 13005, 13006, 13007, 13008, 13009, 13010, 13011, 13012, 13013, 13014, 13015, 13016, 13017, 13018, 13019, 13020, 13021, and 13022, and pharmaceutically acceptable salts and/or solvates thereof. More preferably, the compound of formula (I) is a compound selected from example numbers: 12036, 12038, 12041, 12057, 12060, 12061, 12065, 12068, 2020, 2212, 6601, 6602, 6617, 6618, 6622, 6624, 6626, 6629, 6639, 10901, 10904, 10925, 10926, 10928, 10930, 10931, 10964, 10972, 12001, 12007, 12008, 12009, 12014, 12015, 12016, 12017, 12018, 12019, 12021, 12022, 12023, 12028, 12034, 12035, 12039, 12040, 12042, 12044, 12047, 12048, 12049, 12050, 12051, 12052, 12053, 12054, 12055, 12056, 12058, 12059, 12062, 12064, 12067, 12069, 12070, 12071, 13001, 13006, 13009, 13012, 13020, 13022, 1001, 1002, 1002.1, 1006, 1017, 1133, 1134, 2022, 2211, 5003, 6609, 6614, 6621, 6628, 6630, 6631, 6633, 6637, 6640, 6641, 6642, 6650, 7703, 8806, 10906, 10910, 10920, 10923, 10924, 10932, 10940, 10942, 10953, 11001, 12010, 12012, 12020, 12024, 12026, 12027, 12031, 13003, 13004, 13005, 13007, 13010, 13013, 13014, and 13015, and pharmaceutically acceptable salts and/or solvates thereof. Even more preferably, the compound of formula (I) is a compound selected from example numbers: 12036, 12038, 12041, 12057, 12060, 12061, 12065, 12068, 2020, 2212, 6601, 6602, 6617, 6618, 6622, 6624, 6626, 6629, 6639, 10901, 10904, 10925, 10926, 10928, 10930, 10931, 10964, 10972, 12001, 12007, 12008, 12009, 12014, 12015, 12016, 12017, 12018, 12019, 12021, 12022, 12023, 12028, 12034, 12035, 12039, 12040, 12042, 12044, 12047, 12048, 12049, 12050, 12051, 12052, 12053, 12054, 12055, 12056, 12058, 12059, 12062, 12064, 12067, 12069, 12070, 12071, 13001, 13006, 13009, 13012, 13020, and 13022, and pharmaceutically

acceptable salts and/or solvates thereof. Yet more preferably, the compound of formula (I) is a compound selected from example numbers: 12036, 12038, 12041, 12057, 12060, 12061, 12065, and 12068, and pharmaceutically acceptable salts and/or solvates thereof. Yet more preferably still, the compound of formula (I) is a compound selected from example numbers 1001, 1002.1, 2020, 2022, 6602, 6624, 10901, 10906, 12001, and 12016, and pharmaceutically acceptable salts and/or solvates thereof. More preferably still, the compound of formula (I) is a compound selected from example numbers 1001, 1002.1, 2020, 2022, 6602, 6624, 10901, 10906, and 12001, and pharmaceutically acceptable salts and/or solvates thereof.

Preferably, the compound of formula (I) is a compound selected from example numbers: 1001, 1002, 1002.1, 1002.2, 1004, 1005.1, 1006, 1009, 1011, 1012, 1013, 1014, 1015, 1016, 1017, 1018, 1019, 2020, 2022, 1101, 1105, 1109, 1110, 1113, 1118, 4401, 6601, 6602, 7702, and 10901, and pharmaceutically acceptable salts and/or solvates thereof. More preferably, the compound of formula (I) is a compound selected from example numbers: 1001, 1002, 1002.1, 1006, 1017, 2020, 2022, 6601, 6602, and 10901, and pharmaceutically acceptable salts and/or solvates thereof. Even more preferably, the compound of formula (I) is a compound selected from example numbers: 1001, 1002, and 1005.1, and pharmaceutically acceptable salts and/or solvates thereof. Yet more preferably, the compound of formula (I) is a compound selected from example numbers: 1001 and 1002, and pharmaceutically acceptable salts and/or solvates thereof. Yet more preferably still, the compound of formula (I) is a compound selected from example numbers 1001, 1002.1, and 2020, and pharmaceutically acceptable salts and/or solvates thereof.

Preferably, the compound of formula (I) is a compound selected from example numbers: 1001, 1002, 1002.1, 1002.2, 1004, 1005.1, 1012, 1013, 1014, 1015, 1016, 1017, 1018, 1019, 2020, and 2022, and pharmaceutically acceptable salts and/or solvates thereof. More preferably, the compound of formula (I) is a compound selected from example numbers: 1001, 1002, 1002.1, 1017, 2020, and 2022, and pharmaceutically acceptable salts and/or solvates thereof. Even more preferably, the compound of formula (I) is a compound selected from example numbers: 1001, 1002, and 1005.1, and pharmaceutically acceptable salts and/or solvates thereof. Yet more preferably, the compound of formula (I) is a compound selected from example numbers: 1001 and 1002, and pharmaceutically acceptable salts and/or solvates thereof.

Preferably, the compound of formula (I) is a compound selected from example numbers: 1001, 1002, and 1005.1, and pharmaceutically acceptable salts and/or solvates thereof. More preferably, the compound of formula (I) is a compound selected from example numbers: 1001 and 1002, and pharmaceutically acceptable salts and/or solvates thereof.

Therapeutic Applications

As noted above, the compounds (or pharmaceutically acceptable salts and/or solvates thereof), and pharmaceutical compositions comprising the compounds (or pharmaceutically acceptable salts and/or solvates thereof) of the present invention are inhibitors of FXIIa. They are therefore useful in the treatment of disease conditions for which FXIIa is a causative factor.

Accordingly, the present invention provides a compound of the invention (or a pharmaceutically acceptable salt and/or solvate thereof), or a pharmaceutical composition comprising a compound of the invention (or a pharmaceutically acceptable salt and/or solvate thereof), for use in medicine.

The present invention also provides for the use of a compound of the invention (or a pharmaceutically acceptable salt and/or solvate thereof), or a pharmaceutical composition comprising the compound of the invention (or a pharmaceutically acceptable salt and/or solvate thereof), in the manufacture of a medicament for the treatment or prevention of a disease or condition in which FXIIa activity is implicated.

The present invention also provides a method of treatment of a disease or condition in which FXIIa activity is implicated comprising administration to a subject in need thereof a therapeutically effective amount of a compound of the invention (or a pharmaceutically acceptable salt and/or solvate thereof), or a pharmaceutical composition comprising the compound of the invention (or a pharmaceutically acceptable salt and/or solvate thereof).

As discussed above, FXIIa can mediate the conversion of plasma kallikrein from plasma prekallikrein. Plasma kallikrein can then cause the cleavage of high molecular weight kininogen to generate bradykinin, which is a potent inflammatory hormone. Inhibiting FXIIa has the potential to inhibit (or even prevent) plasma kallikrein production. Thus, the disease or condition in which FXIIa activity is implicated can be a bradykinin-mediated angioedema.

The bradykinin-mediated angioedema can be non-hereditary. For example, the non-hereditary bradykinin-mediated angioedema can be selected from non-hereditary angioedema with normal C1 Inhibitor (AE-nC1 Inh), which can be environmental, hormonal, or drug-induced; acquired angioedema; anaphylaxis associated angioedema; angiotensin converting enzyme (ACE or ace) inhibitor-induced angioedema; dipeptidyl peptidase-4 inhibitor-induced angioedema; and tPA-induced angioedema (tissue plasminogen activator-induced angioedema).

Alternatively, and preferably, the bradykinin-mediated angioedema can be hereditary angioedema (HAE), which is angioedema caused by an inherited dysfunction/fault/mutation. Types of HAE that can be treated with compounds according to the invention include HAE type 1, HAE type 2, and normal C1 inhibitor HAE (normal C1 Inh HAE).

The disease or condition in which FXIIa activity is implicated can be selected from vascular hyperpermeability, stroke including ischemic stroke and haemorrhagic accidents; retinal edema; diabetic retinopathy; impaired visual acuity; DME; retinal vein occlusion; and AMD. These conditions can also be bradykinin-mediated.

As discussed above, FXIIa can activate FXIa to cause a coagulation cascade. Thrombotic disorders are linked to this cascade. Thus, the disease or condition in which FXIIa activity is implicated can be a thrombotic disorder. More specifically, the thrombotic disorder can be thrombosis; thromboembolism caused by increased propensity of medical devices that come into contact with blood to clot blood; prothrombotic conditions such as disseminated intravascular coagulation (DIC), Venous thromboembolism (VTE), cancer associated thrombosis, complications caused by mechanical and bioprosthetic heart valves, complications caused by catheters, complications caused by ECMO, complications caused by LVAD, complications caused by dialysis, complications caused by CPB, sickle cell disease, joint arthroplasty, thrombosis induced to tPA, Paget-Schroetter syndrome and Budd-Chari syndrome; atherosclerosis; COVID-19; acute respiratory distress syndrome (ARDS); idiopathic pulmonary fibrosis (IPF); rheumatoid arthritis (RA); and cold-induced urticarial autoinflammatory syndrome.

Surfaces of medical devices that come into contact with blood can cause thrombosis. The compounds (or pharmaceutically acceptable salts and/or solvates thereof) and pharmaceutical compositions of the present invention can be coated on the surfaces of devices that come into contact with blood to mitigate the risk of the device causing thrombosis. For instance, they can lower the propensity these devices to clot blood and therefore cause thrombosis. Examples of devices that come into contact with blood include

vascular grafts, stents, in dwelling catheters, external catheters, orthopedic prosthesis, cardiac prosthesis, and extracorporeal circulation systems.

Other disease conditions for which FXIIa is a causative factor include: neuroinflammation; neuroinflammatory/neurodegenerative disorders such as MS (multiple sclerosis); other neurodegenerative diseases such as Alzheimer's disease, epilepsy and migraine; sepsis; bacterial sepsis; inflammation; vascular hyperpermeability; and anaphylaxis.

Brown adipose tissue (BAT) thermogenic activity can be mediated by the kallikrein-kinin system, and impaired BAT activity is associated with obesity and insulin resistance. Inhibiting FXIIa has the potential to inhibit (or even prevent) BAT activity mediated by the kallikrein-kinin system. The compounds or pharmaceutically acceptable salts and/or solvates thereof) and pharmaceutical compositions of the invention can therefore treat disease conditions such as obesity and diabetes.

Combination Therapy

The compounds of the present invention (or pharmaceutically acceptable salts and/or solvates thereof) may be administered in combination with other therapeutic agents. Suitable combination therapies include any compound of the present invention (or a pharmaceutically acceptable salt and/or solvate thereof) combined with one or more agents selected from agents that inhibit platelet-derived growth factor (PDGF), endothelial growth factor (VEGF), integrin alpha5beta1, steroids, other agents that inhibit FXIIa and other inhibitors of inflammation.

Some specific examples of therapeutic agents that may be combined with the compounds of the present invention include those disclosed in EP2281885A1 and by S. Patel in *Retina*, 2009 Jun;29(6 Suppl):S45-8.

Other suitable combination therapies include a compound of the invention (or a pharmaceutically acceptable salt and/or solvate thereof) combined with one or more agents selected from agents that treat HAE (as defined generally herein), for example bradykinin B2 antagonists such icatibant (Firazyr®); plasma kallikrein inhibitors such as ecallantide (Kalbitor®), lanadelumab (Takhzyro®) and berotralstat (ORLADEYO™); or C1 esterase inhibitor such as Cinryze® and Haegarda® and Berinert® and Ruconest®.

Other suitable combination therapies include a compound of the invention (or a pharmaceutically acceptable salt and/or solvate thereof) combined with one or more agents selected from agents that are antithrombotics (as outlined above), for example other Factor XIIa inhibitors, thrombin receptor antagonists, thrombin inhibitors, factor VIIa inhibitors, factor Xa inhibitors, factor XIa inhibitors, factor IXa

inhibitors, adenosine diphosphate antiplatelet agents (e.g., P2Y12 antagonists), fibrinogen receptor antagonists (e.g. to treat or prevent unstable angina or to prevent reocclusion after angioplasty and restenosis) and aspirin) and platelet aggregation inhibitors.

When combination therapy is employed, the compounds of the present invention and said combination agents may exist in the same or different pharmaceutical compositions, and may be administered separately, sequentially or simultaneously.

The compounds of the present invention can be administered in combination with laser treatment of the retina. The combination of laser therapy with intravitreal injection of an inhibitor of VEGF for the treatment of diabetic macular edema is known (Elman M, Aiello L, Beck R, et al. "Randomized trial evaluating ranibizumab plus prompt or deferred laser or triamcinolone plus prompt laser for diabetic macular edema" Ophthalmology. 27 April 2010).

Definitions

As noted above, the term "alkyl" is a linear saturated hydrocarbon having up to 10 carbon atoms (C_1-C_{10}) or a branched saturated hydrocarbon of between 3 and 10 carbon atoms (C_3-C_{10}); alkyl may optionally be substituted with 1, 2 or 3 substituents independently selected from (C_1-C_6)alkoxy, OH, -NR13R14, -C(=O)OR13, -C(=O)NR13R14, CN, CF_3, halo. As noted above "alkyl^b" is a linear saturated hydrocarbon having up to 10 carbon atoms (C_1-C_{10}) or a branched saturated hydrocarbon of between 3 and 10 carbon atoms (C_3-C_{10}); alkyl^b may optionally be substituted with 1, 2 or 3 substituents independently selected from (C_1-C_6)alkoxy, OH, CN, CF_3, halo. Examples of such alkyl or alkyl^b groups include, but are not limited, to C_1 - methyl, C_2 - ethyl, C_3 - propyl and C_4-n-butyl, C_3 - iso-propyl, C_4 - sec-butyl, C_4 - iso-butyl, C_4 - tert-butyl and C_5 - neo-pentyl, optionally substituted as noted above. More specifically, "alkyl" or "alkyl^b" can be a linear saturated hydrocarbon having up to 6 carbon atoms (C_1-C_6) or a branched saturated hydrocarbon of between 3 and 6 carbon atoms (C_3-C_6), optionally substituted as noted above. Even more specifically, "alkyl" or "alkyl^b" can be a linear saturated hydrocarbon having up to 4 carbon atoms (C_1-C_4) or a branched saturated hydrocarbon of between 3 and 4 carbon atoms (C_3-C_4), optionally substituted as noted above, which is herein called "small alkyl" or "small alkyl^b", respectively. Preferably, "alkyl" or "alkyl^b" can be defined as a "small alkyl" or "small alkyl^b".

"Aryl" and "aryl^b" are as defined above. Typically, "aryl" or "aryl^b" will be optionally substituted with 1, 2 or 3 substituents. Optional substituents are selected from those stated above. Examples of suitable aryl or aryl^b groups include phenyl, biphenyl and naphthyl (each optionally substituted as stated above).

Preferably "aryl" is selected from phenyl, substituted phenyl (wherein said substituents are selected from those stated above) and naphthyl. Most preferably "aryl" is selected from phenyl and substituted phenyl (wherein said substituents are selected from those stated above).

As noted above, the term "cycloalkyl" is a monocyclic saturated hydrocarbon ring of between 3 and 6 carbon atoms (C_3-C_6); cycloalkyl may optionally be substituted with 1 or 2 substituents independently selected from alkyl, (C_1-C_6)alkoxy, OH, CN, CF_3, halo. Examples of suitable monocyclic cycloalkyl groups include cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl, optionally substituted as noted above. More specifically, "cycloalkyl" can be a monocyclic saturated hydrocarbon ring of between 3 and 5 carbon atoms, more specifically, between 3 and 4 carbon atoms, optionally substituted as noted above.

As noted above, the term "alkoxy" is a linear O-linked hydrocarbon of between 1 and 6 carbon atoms (C_1-C_6) or a branched O-linked hydrocarbon of between 3 and 6 carbon atoms (C_3-C_6); alkoxy may optionally be substituted with 1 or 2 substituents independently selected from OH, CN, CF_3, and fluoro. Examples of such alkoxy groups include, but are not limited to, C_1 - methoxy, C_2 - ethoxy, C_3 - n-propoxy and C_4 - n-butoxy for linear alkoxy, and C_3 - iso-propoxy, and C_4 - sec-butoxy and tert-butoxy for branched alkoxy, optionally substituted as noted aboves. More specifically, "alkoxy" can be linear groups of between 1 and 4 carbon atoms (C_1-C_4), more specifically, between 1 and 3 carbon atoms (C_1-C_3). More specifically, "alkoxy" can be branched groups of between 3 and 4 carbon atoms (C_3-C_4), optionally substituted as noted above.

"Halo" can be selected from Cl, F, Br and I. More specifically, halo can be selected from Cl and F.

As noted above, "heteroaryl" is a 5- or 6- membered carbon-containing aromatic ring containing one, two or three ring members that are selected from N, NR8, S, and O; heteroaryl may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, CN, and CF_3. For example, heteroaryl can be selected from thiophene, furan, pyrrole, pyrazole, imidazole, oxazole, isoxazole, thiazole, isothiazole, triazole, oxadiazole, thiadiazole, pyridine, pyridazine, pyrimidine, and pyrazine, optionally substituted as noted above.

"Heteroaryl^a" and "heteroaryl^b" are as defined above. Typically, "heteroaryl^a" or "heteroaryl^b" will be optionally substituted with 1, 2 or 3 substituents. Optional substituents are selected from those stated above. Examples of suitable heteroaryl^a or heteroaryl^b groups include thienyl, furanyl, pyrrolyl, pyrazolyl, imidazoyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, triazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolyl, benzimidazolyl, benzotriazolyl, quinolinyl,

isoquinolinyl, 5-azathianaphthenyl, indolizinyl, isoindolyl, indazolyl, benzothiazolyl, cinnolinyl, quinazolinyl, quinoxalinyl, 1,8-napthyridinyl and phthalazinyl (optionally substituted as stated above). More specifically, "heteroaryl[a]" or "heteroaryl[b]" can be a 9- or 10- membered bi-cyclic ring as defined, and optionally substituted as stated above. Examples of suitable 9- or 10- membered heteroaryl[a] or heteroaryl[b] groups include indolyl, benzimidazolyl, benzotriazolyl, quinolinyl, isoquinolinyl, 5-azathianaphthenyl, indolizinyl, isoindolyl, indazolyl, benzothiazolyl, cinnolinyl, quinazolinyl, quinoxalinyl, 1,8-napthyridinyl and phthalazinyl.

As noted above, "heterocycloalkyl" is a non-aromatic carbon-containing monocyclic ring containing 3, 4, 5, or 6, ring members, wherein at least one ring member is independently selected from N, NR12, S, and O; heterocycloalkyl may be optionally be substituted with 1 or 2 substituents independently selected from alkyl, (C_1-C_6)alkoxy, OH, CN, CF_3, halo. More specifically, "heterocycloalkyl" can be a non-aromatic carbon-containing monocyclic ring containing 3, 4, 5, or 6, ring members, wherein at least one ring member is independently selected from NR12, and O; heterocycloalkyl may be optionally substituted with 1 or 2 substituents independently selected from alkyl (C_1-C_6)alkoxy, OH, CN, CF_3, halo.

The term "O-linked", such as in "O-linked hydrocarbon residue", means that the hydrocarbon residue is joined to the remainder of the molecule *via* an oxygen atom.

In groups such as -$(CH_2)_{0-6}$-A, "-" denotes the point of attachment of the substituent group to the remainder of the molecule.

As is clear from the definitions above, and for the avoidance of any doubt, it will be understood that "Y" is defined above, and does not encompass Yttrium.

As is clear from the definitions above, and for the avoidance of any doubt, it will be understood that "B" is defined above, and does not encompass Boron.

As is clear from the definitions above, and for the avoidance of any doubt, it will be understood that "W" is defined above, and does not encompass Tungsten.

As is clear from the definitions above, and for the avoidance of any doubt, it will be understood that "V" is defined above, and does not encompass Vanadium.

As is clear from the definitions above, and for the avoidance of any doubt, it will be understood that "U" is defined above, and does not encompass Uranium.

"Salt", as used herein (including "pharmaceutically acceptable salt") means a physiologically or toxicologically tolerable salt and includes, when appropriate, pharmaceutically acceptable base addition salts and pharmaceutically acceptable acid addition salts. For example (i) where a compound of the invention contains one or more acidic groups, for example carboxy groups, base addition salts (including pharmaceutically acceptable base addition salts) that can be formed include sodium, potassium, calcium, magnesium and ammonium salts, or salts with organic amines, such as, diethylamine, *N*-methyl-glucamine, diethanolamine or amino acids (e.g. lysine) and the like; (ii) where a compound of the invention contains a basic group, such as an amino group, acid addition salts (including pharmaceutically acceptable acid addition salts) that can be formed include hydrochlorides, hydrobromides, sulfates, phosphates, acetates, citrates, lactates, tartrates, mesylates, succinates, oxalates, phosphates, esylates, tosylates, benzenesulfonates, naphthalenedisulphonates, maleates, adipates, fumarates, hippurates, camphorates, xinafoates, p-acetamidobenzoates, dihydroxybenzoates, hydroxynaphthoates, succinates, ascorbates, oleates, bisulfates, trifluoroacetates and the like.

Hemisalts of acids and bases can also be formed, for example, hemisulfate and hemicalcium salts.

For a review of suitable salts, see "Handbook of Pharmaceutical Salts: Properties, Selection and Use" by Stahl and Wermuth (Wiley-VCH, Weinheim, Germany, 2002).

"Prodrug" refers to a compound which is convertible *in vivo* by metabolic means (e.g. by hydrolysis, reduction or oxidation) to a compound of the invention. Suitable groups for forming prodrugs are described in 'The Practice of Medicinal Chemistry, 2nd Ed. pp561-585 (2003) and in F. J. Leinweber, *Drug Metab. Res.,* 1987, **18**, 379.

The compounds of the invention can exist in both unsolvated and solvated forms. The term 'solvate' is used herein to describe a molecular complex comprising the compound of the invention and a stoichiometric amount of one or more pharmaceutically acceptable solvent molecules, for example, ethanol. The term 'hydrate' is employed when the solvent is water.

Where compounds of the invention exist in one or more geometric, optical, enantiomeric, diastereomeric and tautomeric forms, including but not limited to *cis*- and *trans*-forms, *E*- and *Z*-forms, *R*-, *S*- and *meso*-forms, keto-, and enol-forms. Unless otherwise stated a reference to a particular compound includes all

such isomeric forms, including racemic and other mixtures thereof. Where appropriate such isomers can be separated from their mixtures by the application or adaptation of known methods (e.g. chromatographic techniques and recrystallisation techniques). Where appropriate such isomers can be prepared by the application or adaptation of known methods (e.g. asymmetric synthesis). For example, where compounds of the invention exist as a mixture of stereoisomers, one stereoisomer can be present at a purity of >90% relative to the remaining stereoisomers, or more specifically at a purity of >95% relative to the remaining stereoisomers, or yet more specifically at a purity of >99% relative to the remaining stereoisomers. For example, where compounds of the invention exists in enantiomeric forms, the compound can be >90% enantiomeric excess (ee), or more specifically >95% enantiomeric excess (ee), or yet more specifically, >99% ee.

Unless otherwise stated, the compounds of the invention include compounds that differ only in the presence of one or more isotopically enriched atoms. For example, compounds wherein hydrogen is replaced by deuterium or tritium, or wherein carbon is replaced by ^{13}C or ^{14}C, are within the scope of the present invention. Such compounds are useful, for example, as analytical tools or probes in biological assays.

Methods for the preparation of deuterated isotopes will be readily apparent to those skilled in the art. For example, methods may include the use of deuterated starting materials in the synthesis of the compounds described herein. Deuterated starting materials will be readily available to the skilled person, from standard commercial sources. Methods for making deuterated isotopes and deuterated starting materials may also include deuterium exchange. For example, deuterium exchange may be achieved by mixing the compounds with D_2O.

In the context of the present invention, references herein to "treatment" include references to curative, palliative and prophylactic treatment. For instance, treatment includes preventing the symptoms of the disease conditions for which FXIIa is a causative factor.

Methods

The compounds of the invention may be administered alone or in combination with one or more other compounds of the invention or in combination with one or more other drugs (or as any combination thereof). Generally, they will be administered as a formulation in association with one or more pharmaceutically acceptable excipients. The term 'excipient' is used herein to describe any ingredient other than the compound(s) of the invention which may impart either a functional (i.e., drug release rate

controlling) and/or a non-functional (i.e., processing aid or diluent) characteristic to the formulations. The choice of excipient will to a large extent depend on factors such as the particular mode of administration, the effect of the excipient on solubility and stability, and the nature of the dosage form.

Compounds of the invention intended for pharmaceutical use may be administered as a solid or liquid, such as a tablet, capsule or solution. Pharmaceutical compositions suitable for the delivery of compounds of the present invention and methods for their preparation will be readily apparent to those skilled in the art. Such compositions and methods for their preparation may be found, for example, in Remington's Pharmaceutical Sciences, 19th Edition (Mack Publishing Company, 1995).

Accordingly, the present invention provides a pharmaceutical composition comprising a compound of the invention and a pharmaceutically acceptable carrier, diluent or excipient.

For the treatment of conditions such as retinal vascular permeability associated with diabetic retinopathy and diabetic macular edema, the compounds of the invention may be administered in a form suitable for injection into the ocular region of a patient, in particular, in a form suitable for intra-vitreal injection. It is envisaged that formulations suitable for such use will take the form of sterile solutions of a compound of the invention in a suitable aqueous vehicle. The compositions may be administered to the patient under the supervision of the attending physician.

The compounds of the invention may also be administered directly into the blood stream, into subcutaneous tissue, into muscle, or into an internal organ. Suitable means for parenteral administration include intravenous, intraarterial, intraperitoneal, intrathecal, intraventricular, intraurethral, intrasternal, intracranial, intramuscular, intrasynovial and subcutaneous. Suitable devices for parenteral administration include needle (including microneedle) injectors, needle-free injectors and infusion techniques.

Parenteral formulations are typically aqueous or oily solutions. Where the solution is aqueous, excipients such as sugars (including but not restricted to glucose, manitol, sorbitol, etc.), salts, carbohydrates and buffering agents (preferably to a pH of from 3 to 9), but, for some applications, they may be more suitably formulated as a sterile non-aqueous solution or as a dried form to be used in conjunction with a suitable vehicle such as sterile, pyrogen-free water.

Parenteral formulations may include implants derived from degradable polymers such as polyesters (i.e., polylactic acid, polylactide, polylactide-co-glycolide, polycapro-lactone, polyhydroxybutyrate),

polyorthoesters and polyanhydrides. These formulations may be administered via surgical incision into the subcutaneous tissue, muscular tissue or directly into specific organs.

The preparation of parenteral formulations under sterile conditions, for example, by lyophilisation, may readily be accomplished using standard pharmaceutical techniques well known to those skilled in the art.

The solubility of compounds of the invention used in the preparation of parenteral solutions may be increased by the use of appropriate formulation techniques, such as the incorporation of co-solvents and/or solubility-enhancing agents such as surfactants, micelle structures and cyclodextrins.

Preferably, the compounds of the invention are administered orally. Oral administration may involve swallowing, so that the compound enters the gastrointestinal tract, and/or buccal, lingual, or sublingual administration by which the compound enters the blood stream directly from the mouth.

Formulations suitable for oral administration include solid plugs, solid microparticulates, semi-solids and liquids (including multiple phases or dispersed systems). Exemplary formulations suitable for oral administration include tablets; soft or hard capsules containing multi- or nano-particulates, liquids, emulsions or powders; lozenges (including liquid-filled); chews; gels; fast dispersing dosage forms; films; ovules; sprays; and buccal/mucoadhesive patches.

Liquid (including multiple phases and dispersed systems) formulations include emulsions, solutions, syrups and elixirs. Such formulations may be presented as fillers in soft or hard capsules (made, for example, from gelatin or hydroxypropylmethylcellulose) and typically comprise a carrier, for example, water, ethanol, polyethylene glycol, propylene glycol, methylcellulose, or a suitable oil, and one or more emulsifying agents and/or suspending agents. Liquid formulations may also be prepared by the reconstitution of a solid, for example, from a sachet.

The compounds of the invention may also be used in fast-dissolving, fast-disintegrating dosage forms such as those described in Liang and Chen, Expert Opinion in Therapeutic Patents, 2001, **11 (6)**, 981-986.

The formulation of tablets is discussed in Pharmaceutical Dosage Forms: Tablets, Vol. 1, by H. Lieberman and L. Lachman (Marcel Dekker, New York, 1980).

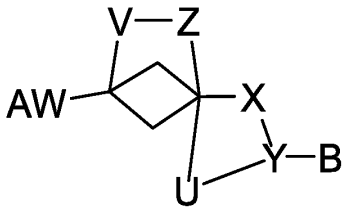
For administration to human patients, the total daily dose of the compounds of the invention is typically in the range 0.1 mg and 10,000 mg, or between 1 mg and 5000 mg, or between 10 mg and 1000 mg depending, of course, on the mode of administration.

The total dose may be administered in single or divided doses and may, at the physician's discretion, fall outside of the typical range given herein. These dosages are based on an average human subject having a weight of about 60kg to 70kg. The physician will readily be able to determine doses for subjects whose weight falls outside this range, such as infants and the elderly.

Numbered embodiments

The invention is also described by the following numbered embodiments:

1. A compound of formula (I),



Formula (I),

wherein:

U is absent, -C(R16)(R17)-, $CH_2C(R16)(R17)$ or $C(R16)(R17)CH_2$;

-V-Z- is:

absent, $-CH_2-$, or $-CH_2-O-CH_2$; or

V is selected from CH_2, O and NR18, and Z is selected from $-C(R16)(R17)-CH_2-$ and -C(R16)(R17)-;

or,

V is selected from $-CH_2-C(R16)(R17)-$ and -C(R16)(R17)-, and Z is selected from CH_2, O and NR18;

wherein R18 is selected from H, alkyl, $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), C(=O)SR19 and SO_2R19;

wherein R19 is selected from alkyl, cycloalkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is selected from a bond, O, CR1R2, C=O and NR12;

Y is, where possible, selected from O, CR1R2, CR1, C=O, N and NR12;

R1 is selected from H, alkyl, alkoxy, OH, halo and NR13R14;

R2 is selected from H and small alkyl;

wherein when one of X or Y is C=O, the other is, where possible, O, CR1R2, CR1, N or NR12;

wherein when X is NR12, Y is, where possible, CR1R2, CR1 or C=O;

wherein when Y is, where possible, NR12 or N, X is a bond, CR1R2 or C=O;

wherein when X is O, Y is, where possible, CR1R2, CR1 or C=O;

wherein when Y, where possible, is O, X is a bond, CR1R2 or C=O;

wherein when X is a bond, Y is, where possible, O, N or NR12;

wherein when U is not absent, -V-Z- is absent;

wherein when -V-Z- is not absent, U is absent;

B is selected from:

(i) heteroaryl[a];

(ii) aryl;

(iii) a 5- to 6- membered non-aromatic heterocyclic ring containing one N ring member, which is unsaturated with 1 or 2 double bonds, wherein the non-aromatic heterocyclic ring is optionally substituted by 1, 2 or 3 substituents independently selected from alkyl, alkoxy, aryl[b], OH, OCF_3, halo, oxo, CN, and CF_3; and

(iv) a fused 5,5-, 6,5- or 6,6- bicyclic ring containing an aromatic ring fused to a non-aromatic ring, wherein the bicyclic ring optionally contains one or two N ring members, wherein the fused 5,5-, 6,5- or 6,6- bicyclic ring may be optionally substituted with 1, 2, or 3 substituted by up to three substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, oxo, CN, and CF_3, wherein the 6,5- bicyclic ring may be attached via the 6- or 5- membered ring;

AW- is selected from:

$-(CH_2)_{0-6}$-(CHR15)-$(CH_2)_{0-6}$-A, -(CHR12)-A, -O-(CHR12)-A, $-(CH_2)_{0-6}$-A, $-(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A, $-(CH_2)_{0-6}$-NH-$(CH_2)_{0-6}$-A, $-(CH_2)_{0-6}$-NR12-$(CH_2)_{1-6}$-C(=O)-A, $-(CH_2)_{0-6}$-NH-C(=O)-$(CH_2)_{0-6}$-A, -C(=O)NR12-$(CH_2)_{0-6}$-A, $-(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A, $-(CH_2)_{0-6}$-(phenyl)-$(CH_2)_{0-6}$-A, -NH-SO_2-A and -SO_2-NH-A;

A is a 4- to 15- membered mono-, bi-, or tri- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN;

wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro;

wherein when A is a tricyclic ring system, each of the three rings in the tricyclic ring system is either fused, bridged or spiro to at least one of the other rings in the tricyclic ring system;

wherein when -V-Z- is -CH_2-, U is absent, and AW- is A-(C=O)-, A may not be substituted by -$(CH_2)_0$-heteroaryl;

alkyl is a linear saturated hydrocarbon having up to 10 carbon atoms (C_1-C_{10}) or a branched saturated hydrocarbon of between 3 and 10 carbon atoms (C_3-C_{10}); alkyl may optionally be substituted with 1, 2 or 3 substituents independently selected from (C_1-C_6)alkoxy, OH, -NR13R14, -C(=O)OR13, -C(=O)NR13R14, CN, CF_3, halo;

$alkyl^b$ is a linear saturated hydrocarbon having up to 10 carbon atoms (C_1-C_{10}) or a branched saturated hydrocarbon of between 3 and 10 carbon atoms (C_3-C_{10}); $alkyl^b$ may optionally be substituted with 1, 2 or 3 substituents independently selected from (C_1-C_6)alkoxy, OH, CN, CF_3, halo;

small alkyl is a linear saturated hydrocarbon having up to 4 carbon atoms (C_1-C_4) or a branched saturated hydrocarbon of between 3 and 4 carbon atoms (C_3-C_4); small alkyl may optionally be substituted with 1 or 2 substituents independently selected from (C1-C6)alkoxy, OH, NR13R14, C(=O)OR13, C(=O)NR13R14, CN, CF_3, halo;

aryl is phenyl, biphenyl or naphthyl; aryl may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, methylenedioxy, ethylenedioxy, OH, halo, CN, -$(CH_2)_{0-3}$-O-$heteroaryl^a$, $aryl^b$, -O-$aryl^b$, -$(CH_2)_{1-3}$-$aryl^b$, -$(CH_2)_{0-3}$-$heteroaryl^a$, -C(=O)OR13, -C(=O)NR13R14, -$(CH_2)_{0-3}$-NR13R14, OCF_3 and CF_3;

$aryl^b$ is phenyl, biphenyl or naphthyl; $aryl^b$ may be optionally substituted with 1, 2 or 3 substituents independently selected from $alkyl^b$, alkoxy, OH, halo, CN, and CF_3;

cycloalkyl is a monocyclic saturated hydrocarbon ring of between 3 and 6 carbon atoms (C_3-C_6); cycloalkyl may optionally be substituted with 1 or 2 substituents independently selected from alkyl, (C_1-C_6)alkoxy, OH, CN, CF_3, halo;

alkoxy is a linear O-linked hydrocarbon of between 1 and 6 carbon atoms (C_1-C_6) or a branched O-linked hydrocarbon of between 3 and 6 carbon atoms (C_3-C_6); alkoxy may optionally be substituted with 1 or 2 substituents independently selected from OH, CN, CF_3, and fluoro;

halo is F, Cl, Br, or I;

heteroaryl is a 5- or 6- membered carbon-containing aromatic ring containing one, two or three ring members that are selected from N, NR8, S, and O; heteroaryl may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, CN, and CF_3;

heteroaryl[a] is a 5, 6, 9 or 10 membered mono- or bi-cyclic aromatic ring, containing, where possible, 1, 2, 3 or 4 ring members independently selected from N, NR12, S and O; heteroaryl[a] may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, CN, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b], -C(=O)OR12, -C(=O)NR13R14 and CF_3;

heteroaryl[b] is a 5, 6, 9 or 10 membered mono- or bi-cyclic aromatic ring, containing, where possible, 1, 2 or 3 ring members independently selected from N, NR12, S and O; wherein heteroaryl[b] may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl[b], alkoxy, OH, halo, CN, aryl[b], $-(CH_2)_{1-3}$-aryl[b], and CF_3;

R8 is independently selected from H, alkyl, cycloalkyl, and heterocycloalkyl;

heterocycloalkyl is a non-aromatic carbon-containing monocyclic ring containing 3, 4, 5, or 6, ring members, wherein at least one ring member is independently selected from N, NR12, S, and O; heterocycloalkyl may be optionally be substituted with 1 or 2 substituents independently selected from alkyl, $(C_1$-$C_6)$alkoxy, OH, CN, CF_3, halo;

R12 is independently selected from H, alkyl, and cycloalkyl;

R13 and R14 are independently selected from H, alkyl[b], aryl[b] and heteroaryl[b] or R13 and R14 together with the nitrogen atom to which they are attached form a carbon-containing 4-, 5-, 6- or 7-membered heterocyclic ring, optionally containing an additional heteroatom selected from N, NR12, S, SO, SO_2, and O, which may be saturated or unsaturated with 1 or 2 double bonds and which may be optionally mono- or di-substituted with substituents selected from oxo, alkyl[b], alkoxy, OH, halo and CF_3;

R15 is selected from alkyl, halo, CF_3, CN, OH, alkoxy, NR13R14, and CONR13R14;

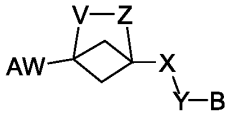
R16 and R17 are independently selected from H and small alkyl;

and tautomers, isomers, stereoisomers (including enantiomers, diastereoisomers and racemic and scalemic mixtures thereof), deuterated isotopes, and pharmaceutically acceptable salts and/or solvates thereof;

wherein the compound is not *N*-(2-chlorophenyl)-3-((5-cyano-1*H*-indazol-1-yl)-methyl)-*N*-methylbicyclo-[1.1.1]pentane-1-carboxamide.

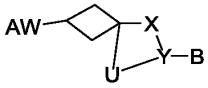
2. A compound of formula (I) according to numbered embodiment 1, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein R18 is selected from alkyl, $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), C(=O)SR19 and SO_2R19.

3. A compound of formula (I) according to any of numbered embodiments 1 to 2, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein U is absent,
which is a compound of formula (1a)



Formula (1a).

4. A compound of formula (I) according to any of numbered embodiments 1 to 2, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein -V-Z- is absent,
which is a compound of formula (1b)

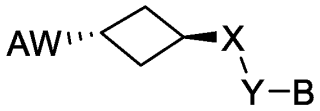


Formula (1b).

5. A compound of formula (I) according to any of numbered embodiments 1 to 4, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein when -V-Z- is absent and U is absent, and AW- and -XYB are trans to one another

which is a compound of formula (1c)



Formula (1c).

6. A compound of formula (I) according to any of numbered embodiments 1 to 3, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein, when not absent, -V-Z- is selected from:

$-CH_2-$, or

V is selected from CH_2, O and NR18, and Z is selected from $-C(R16)(R17)-CH_2-$ and $-C(R16)(R17)-$; or,

V is selected from $-CH_2-C(R16)(R17)-$ and $-C(R16)(R17)-$, and Z is selected from CH_2, O and NR18; or wherein when -V-Z- is absent:

U is absent, CH_2 or $-CH_2CH_2-$.

7. A compound of formula (I) according to any of numbered embodiments 1 to 3, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$; or

when -V-Z- is absent:

U is absent, CH_2 or $-CH_2CH_2-$.

8. A compound of formula (I) according to any of numbered embodiments 1 to 3, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$; or

when -V-Z- is absent:

U is absent, CH_2 or $-CH_2CH_2-$.

9. A compound of formula (I) according to any of numbered embodiments 1 to 3, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or

wherein when -V-Z- is absent:

U is absent, CH_2 or $-CH_2CH_2-$.

10. A compound of formula (I) according to any of numbered embodiments 1 to 3, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or

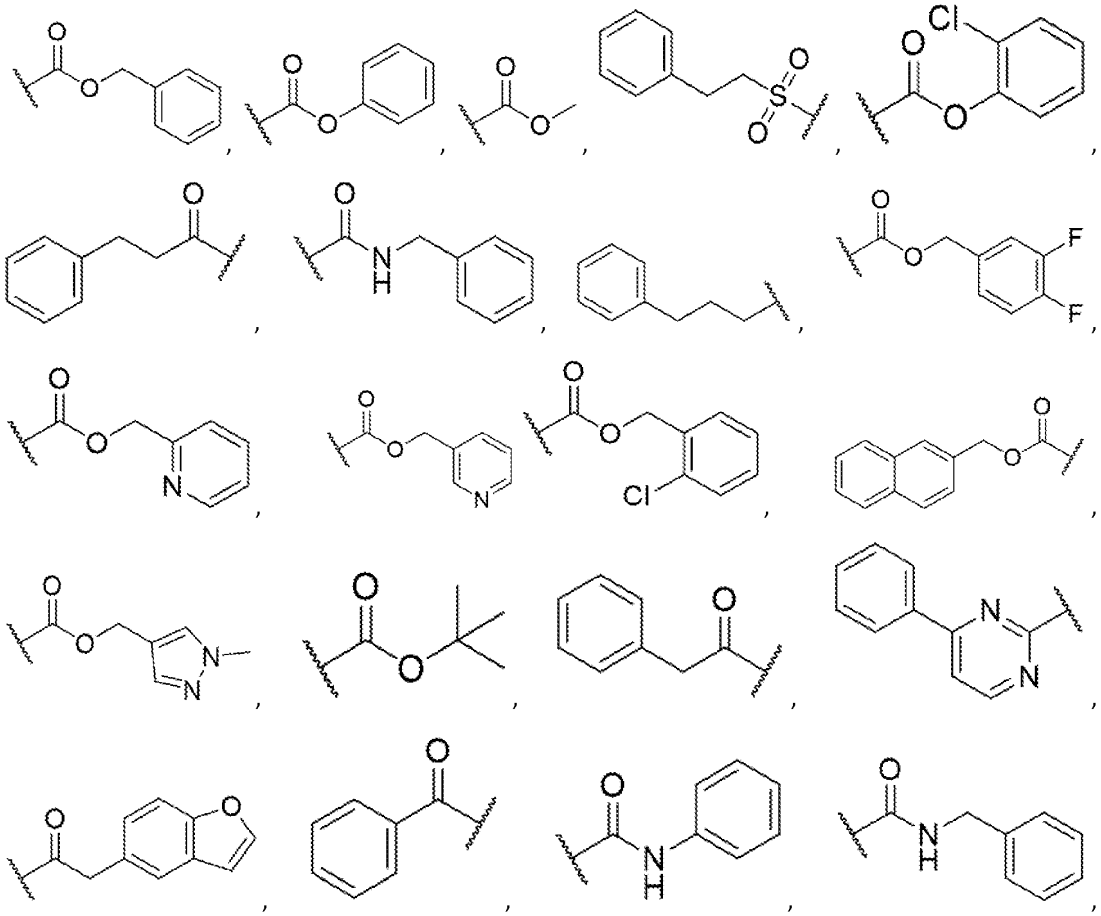
wherein when -V-Z- is absent:

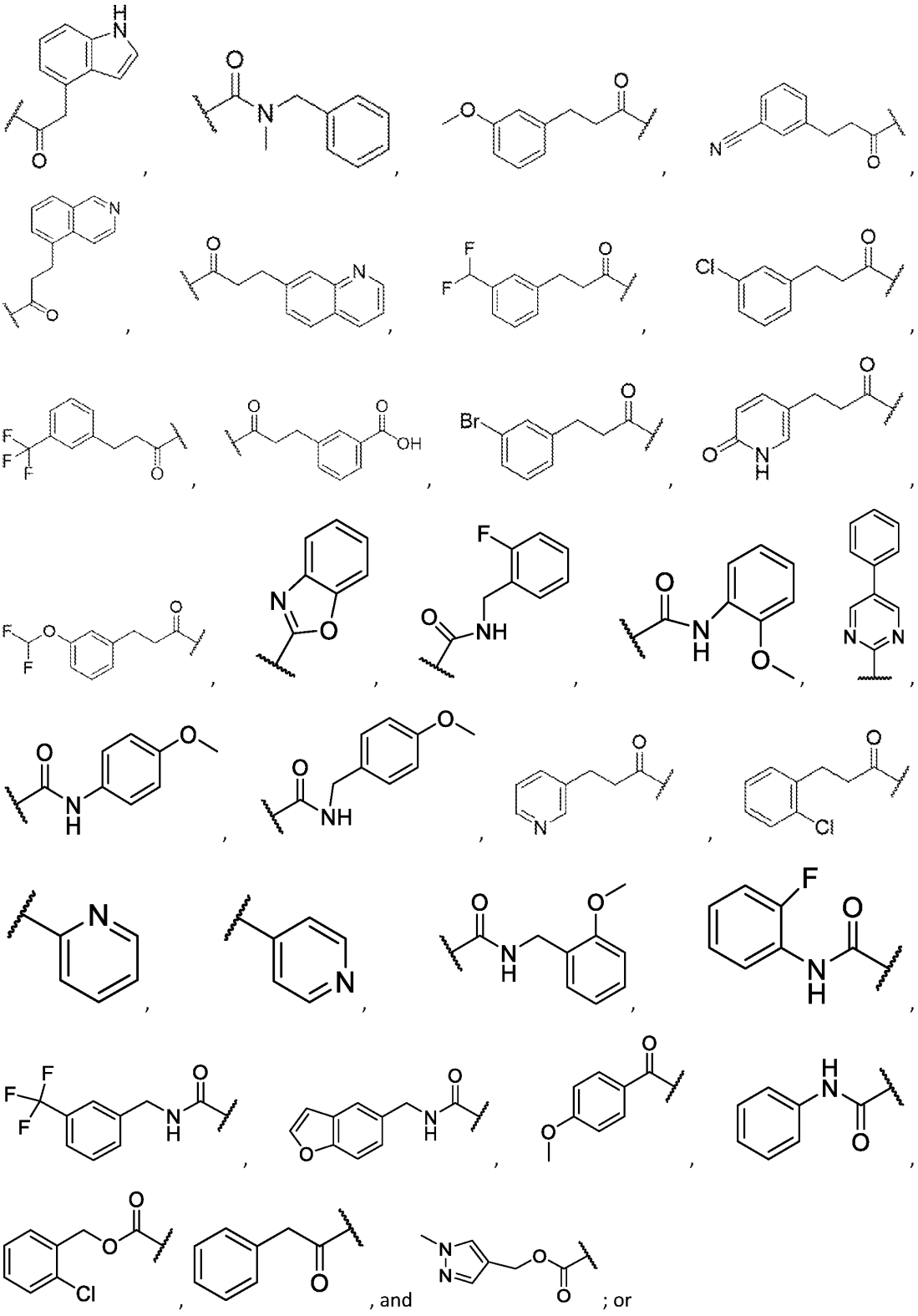
U is absent, CH_2 or $-CH_2CH_2-$.

11. A compound of formula (I) according to any of numbered embodiments 1 to 3, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from:





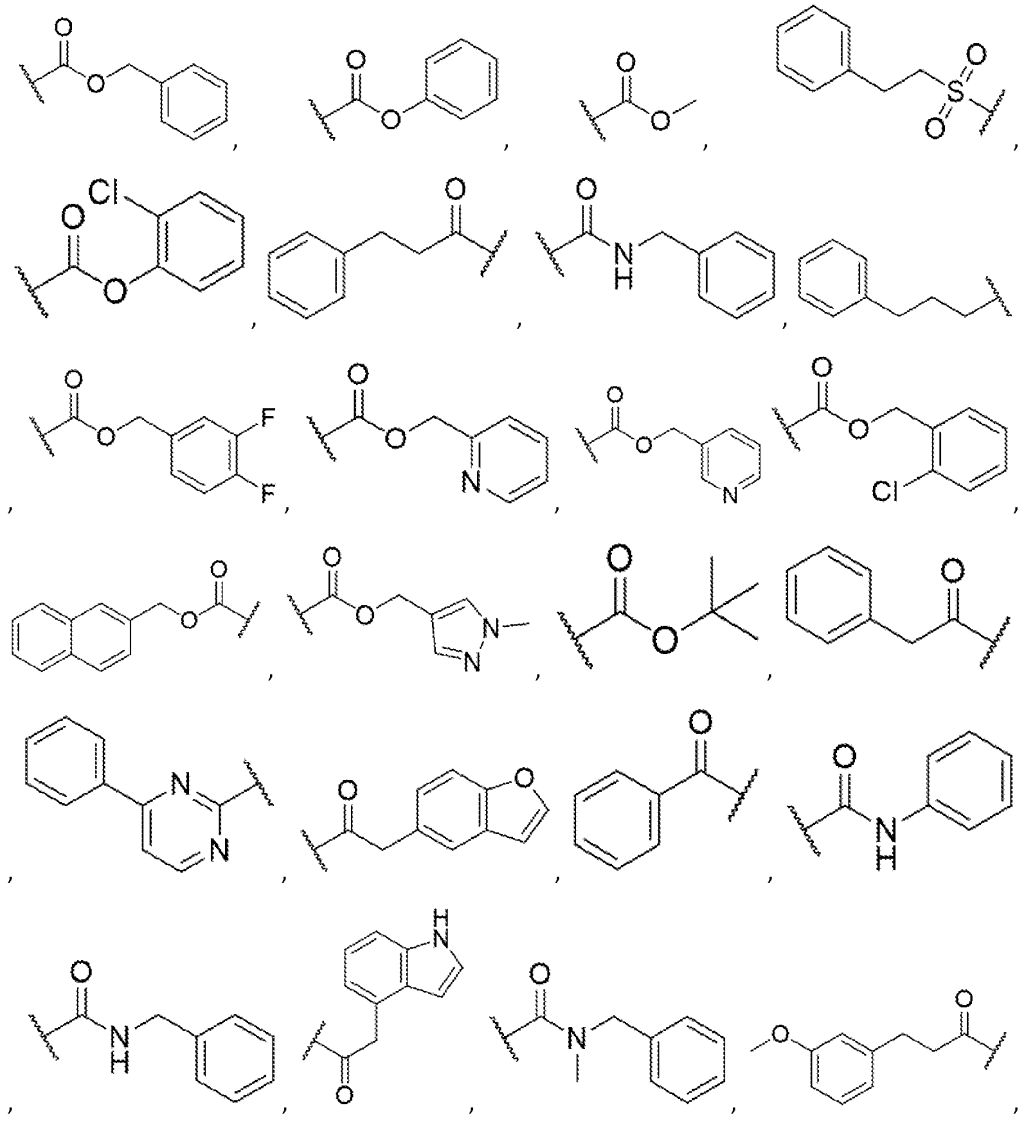
wherein when -V-Z- is absent:

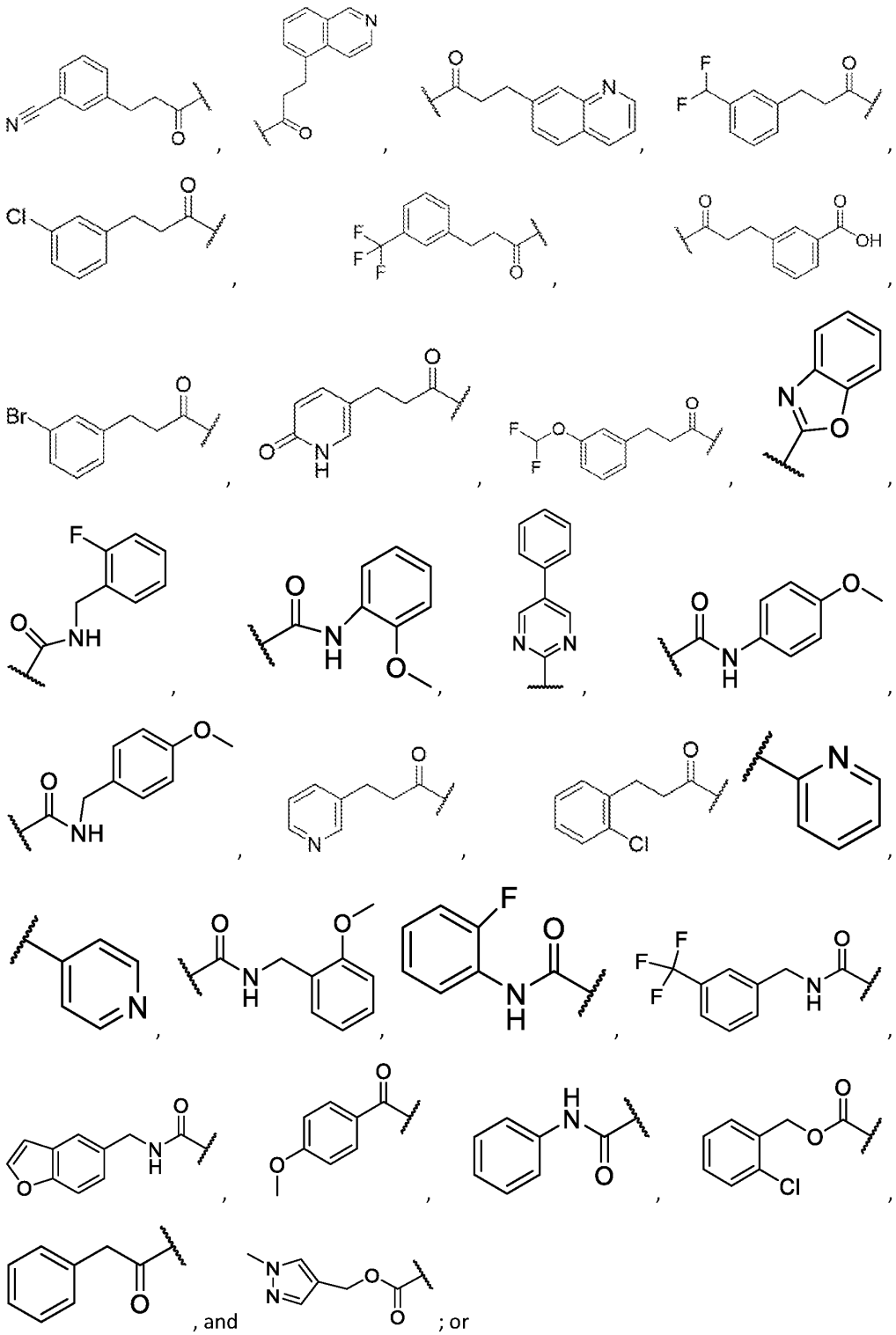
U is absent, CH_2 or $-CH_2CH_2-$.

12. A compound of formula (I) according to any of numbered embodiments 1 to 3, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from:





, and ; or

wherein when -V-Z- is absent:

U is absent, CH_2 or $-CH_2CH_2-$.

13. A compound of formula (I) according to any of numbered embodiments 1 to 2, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or,

wherein when -V-Z- is absent:

U is absent, CH_2 or $-CH_2CH_2-$.

14. A compound of formula (I) according to numbered embodiment 6, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or

when -V-Z- is absent:

U is absent, CH_2 or $-CH_2CH_2-$.

15. A compound of formula (I) according to numbered embodiment 6, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

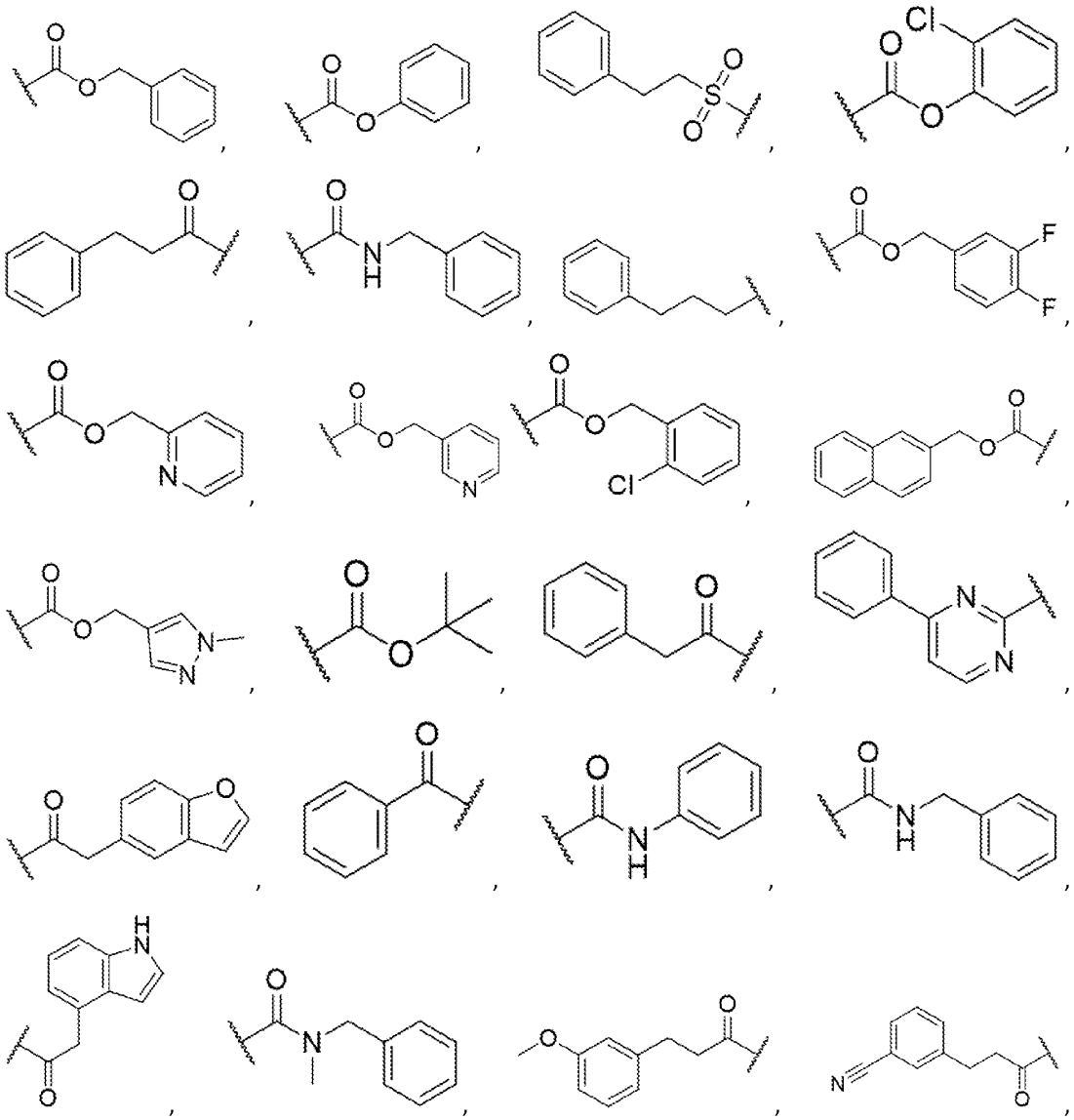
wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or

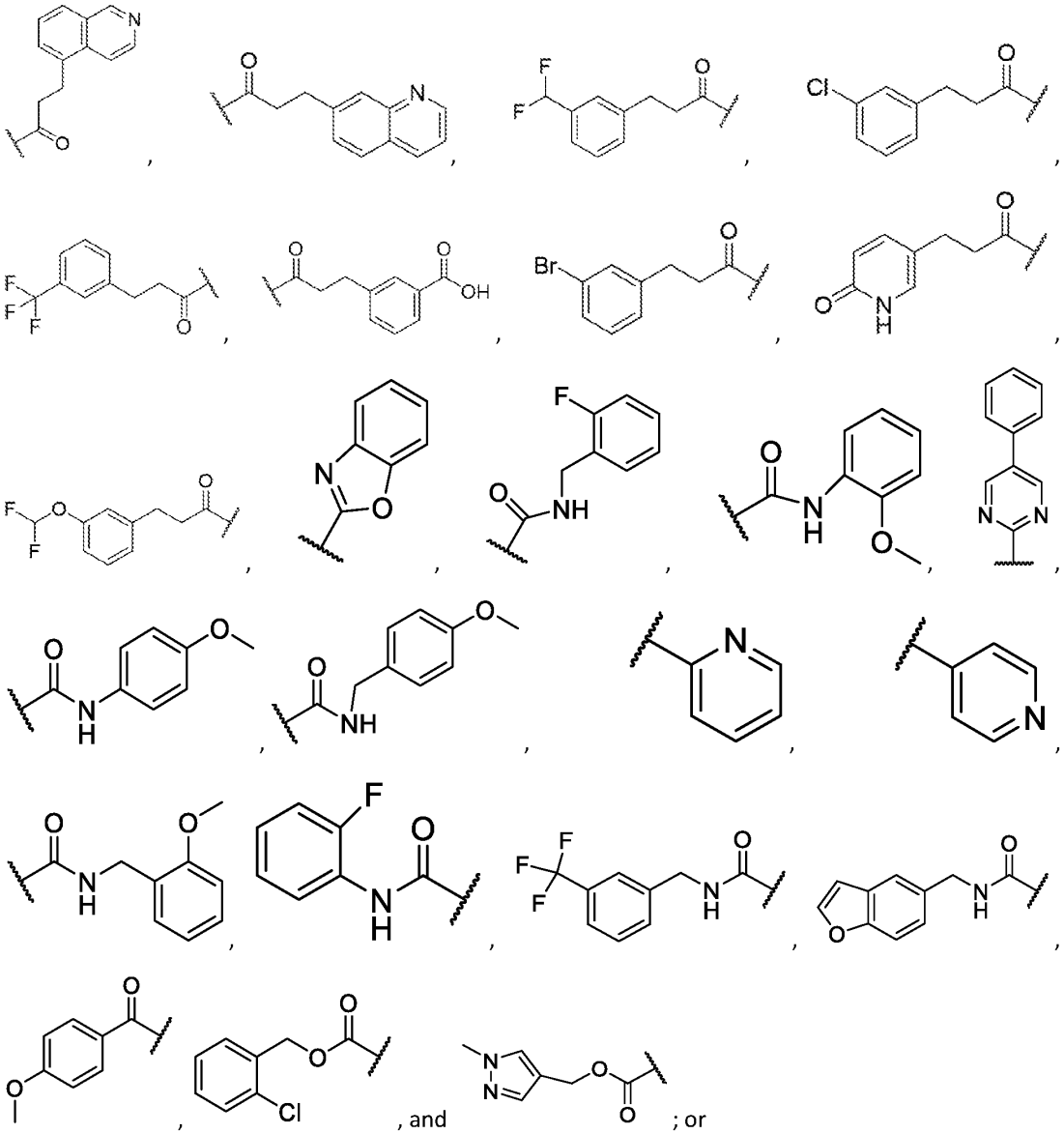
when -V-Z- is absent:

U is absent, CH_2 or $-CH_2CH_2-$.

16. A compound of formula (I) according to numbered embodiment 6, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from:





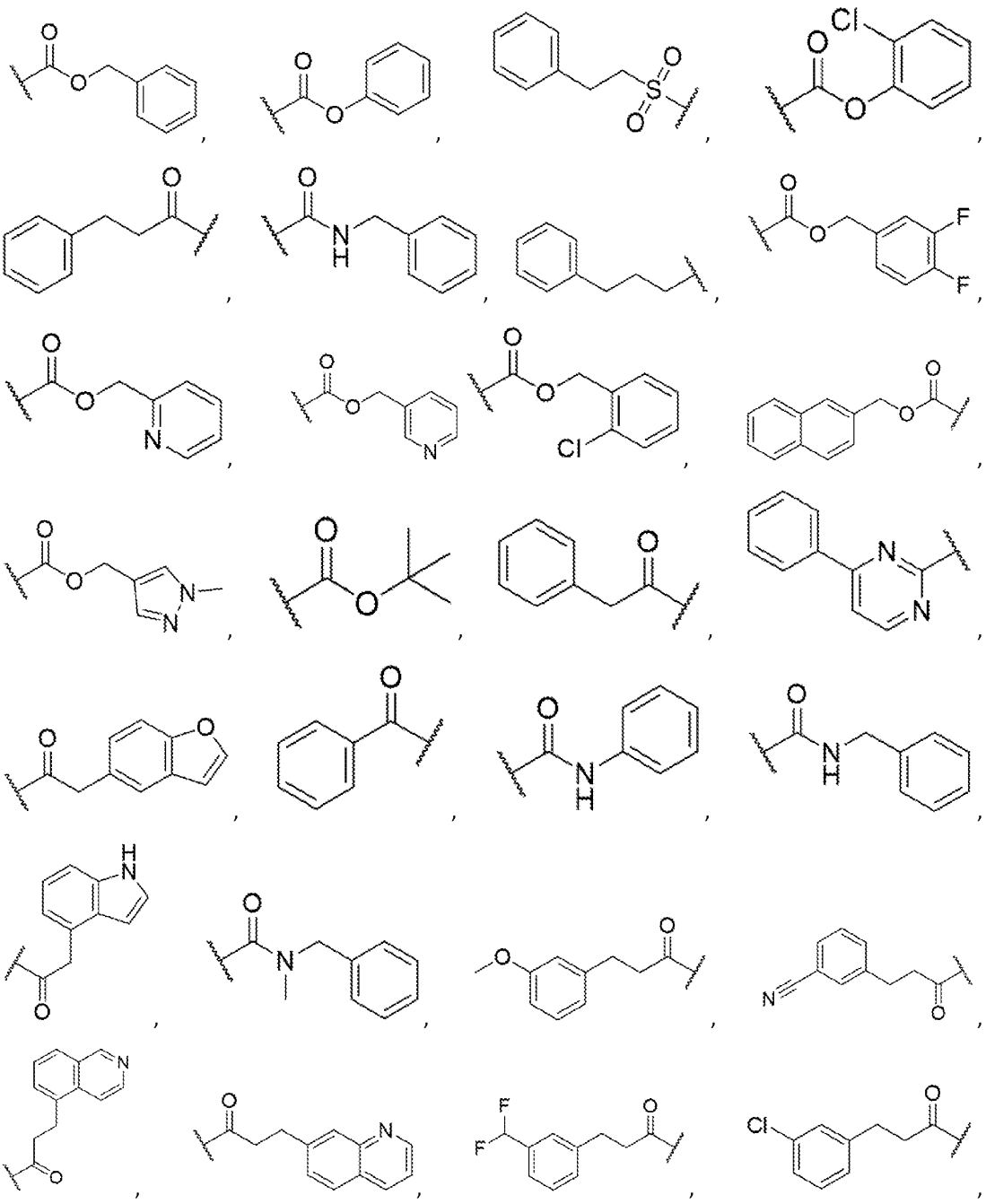
wherein when -V-Z- is absent:

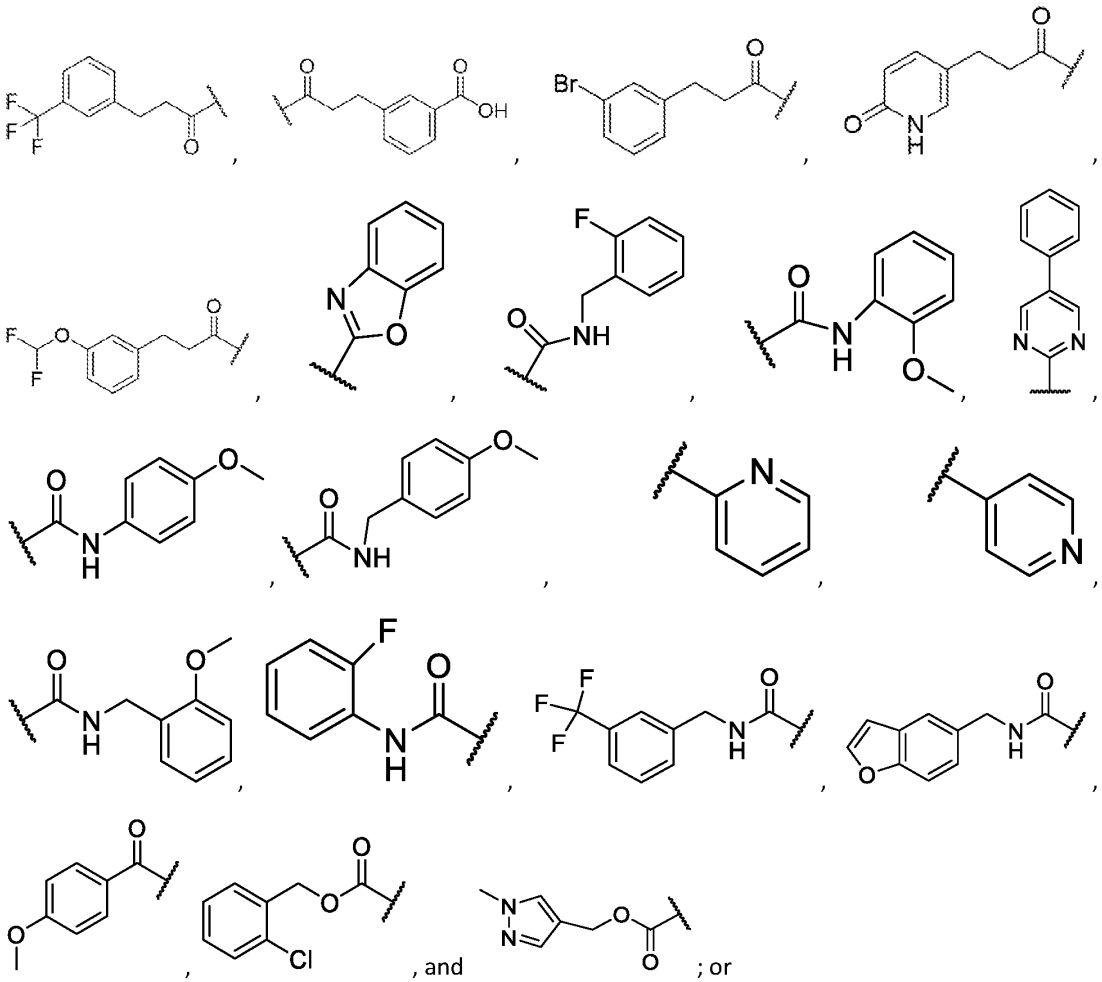
U is absent, CH_2 or $-CH_2CH_2-$.

17. A compound of formula (I) according to numbered embodiment 6, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-N(COCH_3)-CH_2$,

-CH_2-N($COCH_3$), -CH_2-CH_2-, -CH_2-CH_2-O-, -CH_2-CH_2-CH_2-, -CH_2-N(R18)- and -N(R18)-CH_2- wherein R18 is selected from:





wherein when -V-Z- is absent:

U is absent, CH_2 or $-CH_2CH_2-$.

18. A compound of formula (I) according to numbered embodiment 13, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein, when not absent, -V-Z- is selected from:

$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or,

wherein when -V-Z- is absent:

U is absent, CH_2 or $-CH_2CH_2-$.

19. A compound of formula (I) according to numbered embodiment 6, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-

wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or

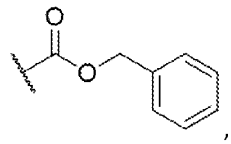
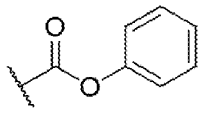
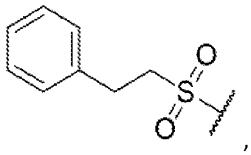
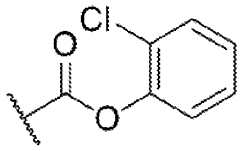
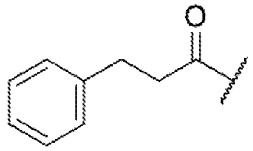
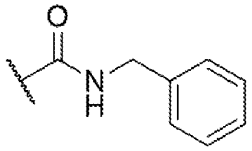
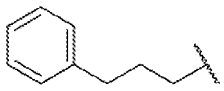
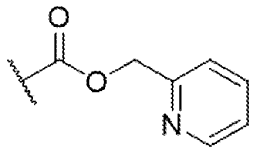
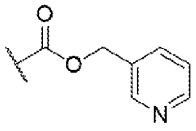
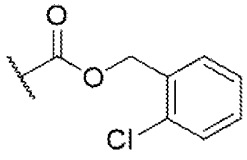
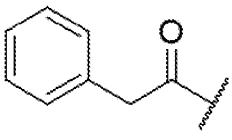
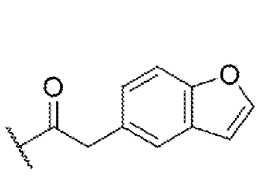
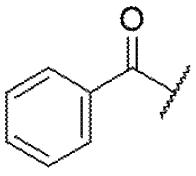
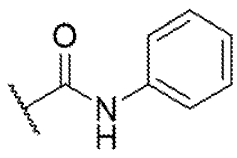
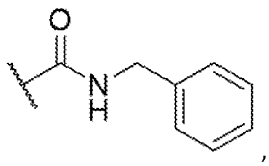
when -V-Z- is absent:

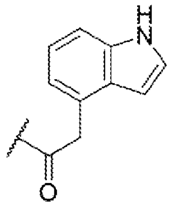
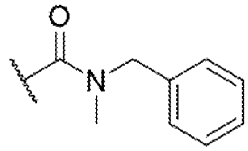
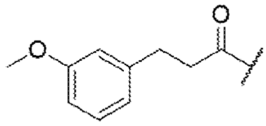
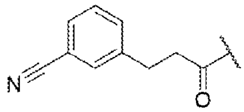
U is absent, CH_2 or -CH_2CH_2-.

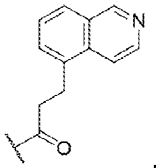
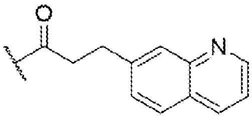
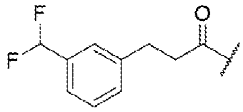
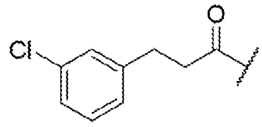
20. A compound of formula (I) according to numbered embodiment 6, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

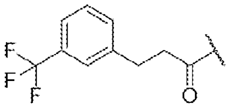
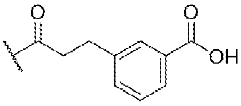
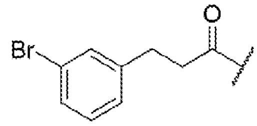
wherein -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O-, -CH_2-CH_2-O-, -CH_2-N(R18)- and -N(R18)-CH_2-

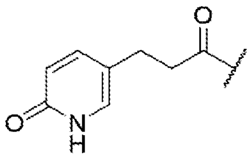
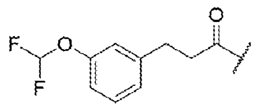
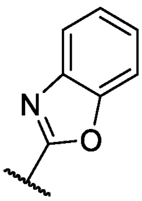
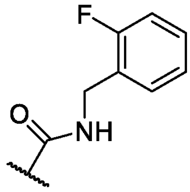
wherein R18 is selected from:

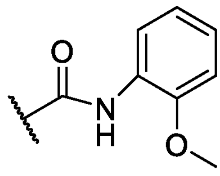
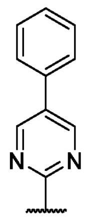
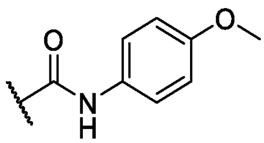
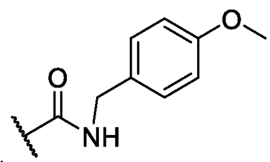
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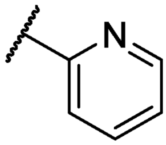
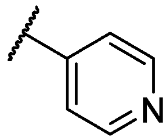
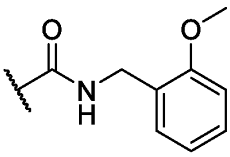
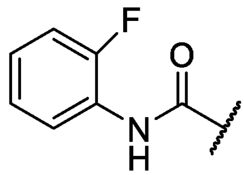
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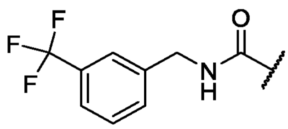
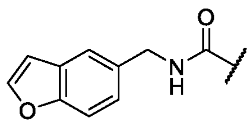
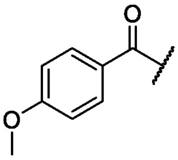
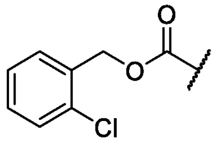
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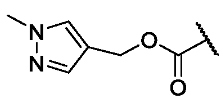
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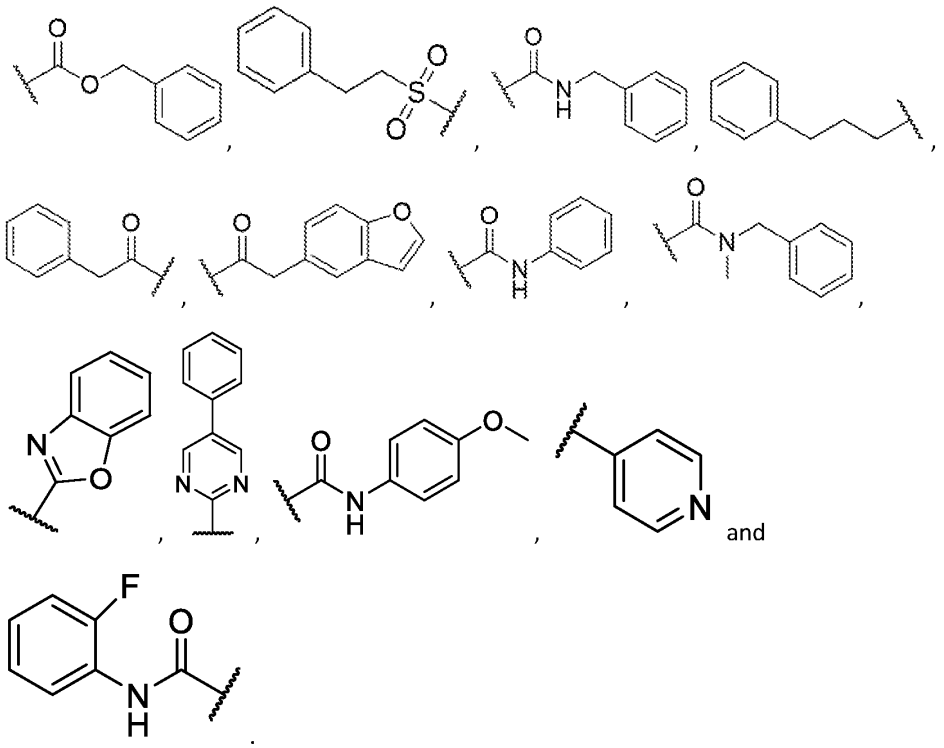
and  .

21. A compound of formula (I) according to numbered embodiment 6, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein -V-Z- is selected from $-CH_2-$, $-O-CH_2-$, $-CH_2-O-$, $-CH_2-CH_2-O-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from:

$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;

wherein R19 is selected from $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a].

22. A compound of formula (I) according to numbered embodiment 6, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein -V-Z- is selected from $-CH_2-$, $-O-CH_2-$, $-CH_2-O-$, $-CH_2-CH_2-O-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$ wherein R18 is selected from:



and

23. A compound of formula (I) according to numbered embodiment 18, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein -V-Z- is selected from -CH_2-, -O-CH_2-, -CH_2-O- and -CH_2-CH_2-O-.

24. A compound of formula (I) according to numbered embodiment 6, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein -V-Z- is selected from -O-CH_2- and -CH_2-O-.

25. A compound of formula (I) according to any of numbered embodiment 1, 2 or 3, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein:

U is absent;

X and Y are independently selected from O, CR1R2, C=O and NR12;

wherein when one of X or Y is C=O, the other is O, CR1R2 or NR12;

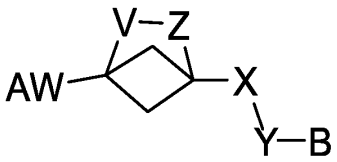
wherein when one of X or Y is NR12, the other is CR1R2 or C=O;

wherein when one of X or Y is O, the other is CR1R2 or C=O;

-V-Z- is -CH_2- or;

V is O and Z is CR16R17;

which is a compound of formula (1d)

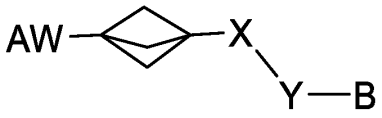


Formula (1d).

26. A compound of formula (I) according to any of numbered embodiments 1 to 3, or 6 to 23, or 25, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein U is absent and -V-Z- is -CH_2-

which is a compound of formula (1e)

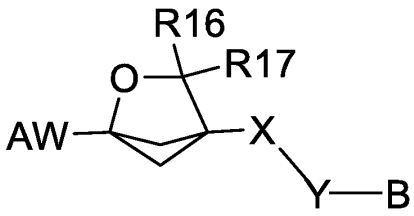


Formula (1e).

27. A compound of formula (I) according to any of numbered embodiments 1 to 3, or 25, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein U is absent, V is O and Z is CR16R17

which is a compound of formula (1f)



Formula (1f).

28. A compound of formula (I) according to numbered embodiment 27, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein R16 and R17 are both H, or R16 and R17 are both $-CH_3$.

29. A compound of formula (I) according to numbered embodiment 28, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein R16 and R17 are both H.

30. A compound of formula (I) according to any of numbered embodiments 1 to 24, or 26 to 29, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein X is selected from a bond and CR1R2.

31. A compound of formula (I) according to numbered embodiment 30, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein X is selected from a bond and CH_2.

32. A compound of formula (I) according to numbered embodiment 31, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein X is CH_2.

33. A compound of formula (I) according to numbered embodiment 31, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein X is CH_2, and Y is, where possible, N or NR12.

34. A compound of formula (I) according to numbered embodiment 31, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein X is CH_2, and Y is, where possible, N or NH.

35. A compound of formula (I) according to numbered embodiment 31, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein X is CH_2, Y is NR12, and U is absent.

36. A compound of formula (I) according to numbered embodiment 31, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein X is CH_2, Y is NH and U is absent.

37. A compound of formula (I) according to any of numbered embodiments 1 to 24, or 26 to 32, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein Y is, where possible, selected from O, CR1R2, N and NR12.

38. A compound of formula (I) according to numbered embodiment 37, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein Y is, where possible, selected from O, CH_2, N and NH.

39. A compound of formula (I) according to any of numbered embodiments 1 to 3, 13 to 24, or 30 to 38 , or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein:
-V-Z- is -CH_2-, X is CH_2 and Y is NH;
-V-Z- is -O-CH_2-, X is CH_2 and Y is NH;
-V-Z- is -CH_2-O-, X is CH_2 and Y is NH; or
-V-Z- is -CH_2-CH_2-O-, X is CH_2 and Y is NH.

40. A compound of formula (I) according to any of numbered embodiments 1 to 29, or 37 to 38, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein X is C=O.

41. A compound of formula (I) according to any of numbered embodiments 1 to 29, or 37 to 38, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein X is NR12.

42. A compound of formula (I) according to any of numbered embodiments 1 to 30, or 37 to 17 , or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein X is CR1R2.

43. A compound of formula (I) according to any of numbered embodiments 1 to 29, or 37 to 38, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein X is O.

44. A compound of formula (I) according to any one of numbered embodiments 1 to 23, 26 to 31, or 37 to 38, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein X is a bond.

45. A compound of formula (I) according to any of numbered embodiments 1 to 29, 32, or 41 to 43, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein Y is, where possible, C=O.

46. A compound of formula (I) according to any of numbered embodiments 1 to 37, 40, 42, or 44, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein Y is, where possible, NR12 or N.

47. A compound of formula (I) according to any of numbered embodiments 1 to 37, 40, 42, or 44, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein Y is, where possible, NR12.

48. A compound of formula (I) according to any of numbered embodiments 1 to 30, 32 to 37, 40 to 44, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein Y is, where possible, CR1R2.

49. A compound of formula (I) according to any of numbered embodiments 1 to 38, 40, 42 or 44, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein Y is, where possible, O.

50. A compound of formula (I) according to any of numbered embodiments 1, 28 to 38, 40, 42 or 44, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein Y is, where possible, N.

51. A compound of formula (I) according to numbered embodiment 41 or 47, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein NR12 is NH.

52. A compound of formula (I) according to numbered embodiment 41, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein X is NH.

53. A compound of formula (I) according to numbered embodiment 47, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein Y is, where possible, NH.

54. A compound of formula (I) according to any of numbered embodiments 42 or 48, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein R1 is H.

55. A compound of formula (I) according to numbered embodiment 42, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein X is CHR2.

56. A compound of formula (I) according to numbered embodiment 48, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein Y is, where possible, CHR2.

57. A compound of formula (I) according to any of numbered embodiments 42, 48, or 54, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein R2 is H.

58. A compound of formula (I) according to numbered embodiment 42, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein X is CR1H.

59. A compound of formula (I) according to numbered embodiment 48, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein Y is, where possible, CR1H.

60. A compound of formula (I) according to any of numbered embodiments 55 or 58, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein X is CH_2.

61. A compound of formula (I) according to any of numbered embodiments 56 or 59, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic

mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein Y is, where possible, CH_2.

62. A compound of formula (I) according to any preceding numbered embodiment, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein B is selected from heteroaryl[a] and aryl.

63. A compound of formula (I) according to numbered embodiment 62, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein B is heteroaryl[a].

64. A compound of formula (I) according to numbered embodiment 63 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein Y is attached to B at a carbon atom on the heteroaryl[a] ring.

65. A compound of formula (I) according to numbered embodiment 63 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein Y is attached to B at a carbon atom on the heteroaryl[a] ring, and the two ring atoms adjacent to the carbon atom on the heteroaryl[a] ring to which Y attaches are both carbon.

66. A compound of formula (I) according to any of numbered embodiments 63 to 65, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein B is a 9 or 10 membered bicyclic aromatic ring, containing, where possible, 1, 2, 3 or 4 ring members independently selected from N, NR12, S and O, optionally substituted as for hereroaryl[a].

67. A compound of formula (I) according to any of numbered embodiments 63 to 66, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

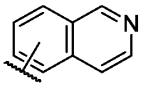
wherein B is a 9 or 10 membered bicyclic aromatic ring, containing 1 or 2 ring members independently selected from N or NR12, optionally substituted as for hereroaryl[a].

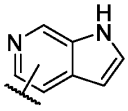
68. A compound of formula (I) according to numbered embodiment 67, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein B is:

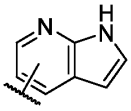
isoquinolinyl, optionally substituted as for heteroaryl[a], or

azaindole, optionally substituted as for heteroaryl[a].

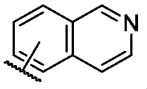
69. A compound of formula (I) according to numbered embodiment 68 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein B is selected from:

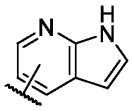
isoquinolinyl  , optionally substituted as for heteroaryl[a];

6-azaindolyl  , optionally substituted as for heteroaryl[a]; and

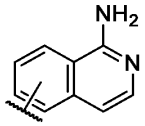
7-azaindolyl  , optionally substituted as for heteroaryl[a].

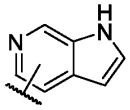
70. A compound of formula (I) according to numbered embodiment 69 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein B is selected from:

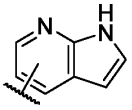
isoquinolinyl  , optionally substituted as for heteroaryl[a]; and

7-azaindolyl  , optionally substituted as for heteroaryl[a].

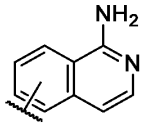
71. A compound of formula (I) according to numbered embodiment 69 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein B is selected from:

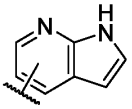
isoquinolinyl, substituted with NH_2 at the 1- position  , optionally further substituted with 1 or 2 substituents as for heteroaryl[a];

6-azaindolyl  , optionally substituted as for heteroaryl[a]; and

7-azaindolyl  , optionally substituted as for heteroaryl[a].

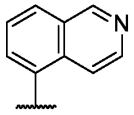
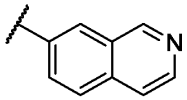
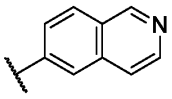
72. A compound of formula (I) according to numbered embodiment 68 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein B is selected from:

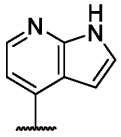
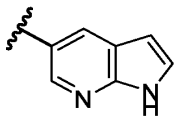
isoquinolinyl, substituted with NH_2 at the 1- position  , optionally further substituted with 1 or 2 substituents as for heteroaryl[a]; and

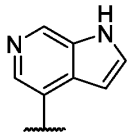
7-azaindolyl  , optionally substituted as for heteroaryl[a].

73. A compound of formula (I) according to numbered embodiment 68 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

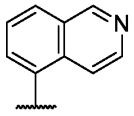
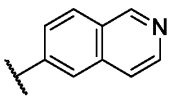
wherein B is selected from:

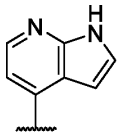
isoquinolinyl, selected from  ,  and  , optionally substituted as for heteroaryl[a];

7-azaindolyl  and  , optionally substituted as for heteroaryl[a]; and

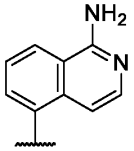
6-azaindolyl  , optionally substituted as for heteroaryl[a].

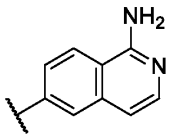
74. A compound of formula (I) according to numbered embodiment 68 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein B is selected from:

isoquinolinyl, selected from  and  , optionally substituted as for heteroaryl[a]; and

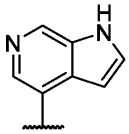
7-azaindolyl  optionally substituted as for heteroaryl[a].

75. A compound of formula (I) according to numbered embodiment 68 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein B is selected from:

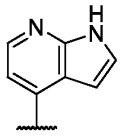
isoquinolinyl, substituted with NH_2 at the 1- position, selected from  and

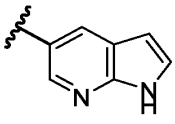


, optionally further substituted with 1 or 2 substituents as for heteroaryl[a];

6-azaindolyl 

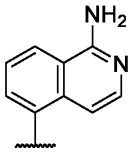
, optionally substituted as for heteroaryl[a]; and

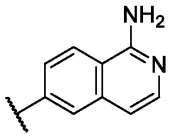
7-azaindolyl selected from 

and 

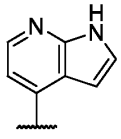
, optionally substituted as for heteroaryl[a].

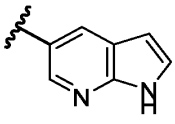
76. A compound of formula (I) according to numbered embodiment 68 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein B is selected from:

isoquinolinyl, substituted with NH_2 at the 1- position, selected from 

and 

, optionally further substituted with 1 or 2 substituents as for heteroaryl[a]; and

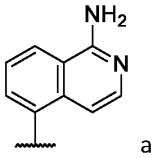
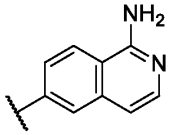
7-azaindolyl selected from 

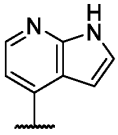
and 

, optionally substituted as for heteroaryl[a].

77. A compound of formula (I) according to numbered embodiment 68 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

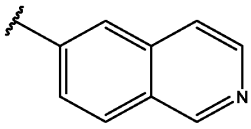
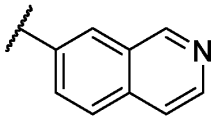
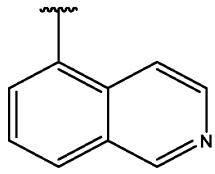
wherein B is selected from:

isoquinolinyl, substituted with NH_2 at the 1- position, selected from  and  , optionally further substituted with 1 or 2 substituents as for heteroaryl[a]; and

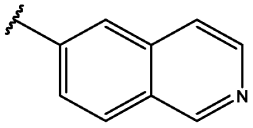
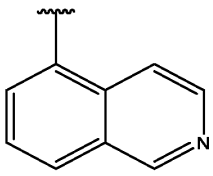
7-azaindolyl  , optionally substituted as for heteroaryl[a].

78. A compound of formula (I) according to numbered embodiment 68, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein B is isoquinolinyl, optionally substituted as for heteroaryl[a].

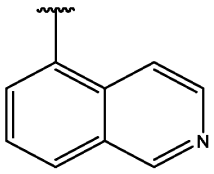
79. A compound of formula (I) according to numbered embodiment 78, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein B is isoquinolinyl, wherein B can be selected from

 ,  and  , optionally substituted as for heteroaryl[a].

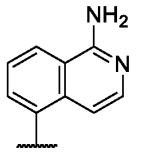
80. A compound of formula (I) according to numbered embodiment 79, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein B is isoquinolinyl, wherein B can be selected from

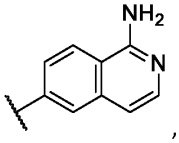

, and 
, optionally substituted as for heteroaryl[a].

81. A compound of formula (I) according to numbered embodiment 79, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein B is isoquinolinyl, wherein B can be

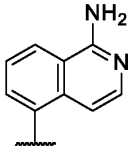

, optionally substituted as for heteroaryl[a].

82. A compound of formula (I) according to numbered embodiment 79 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein B is:

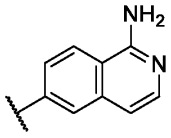
isoquinolinyl, substituted with NH_2 at the 1- position, selected from 
and


, optionally further substituted with 1 or 2 substituents as for heteroaryl[a].

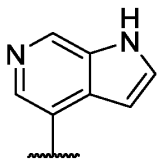
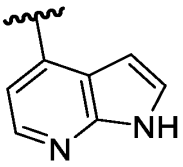
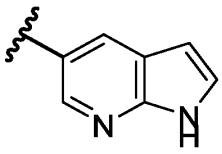
83. A compound of formula (I) according to numbered embodiment 79 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein B is:

isoquinolinyl, substituted with NH_2 at the 1- position 
, optionally further substituted with 1 or 2 substituents as for heteroaryl[a].

84. A compound of formula (I) according to numbered embodiment 79 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein B is:

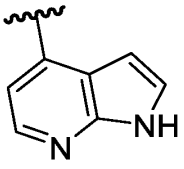
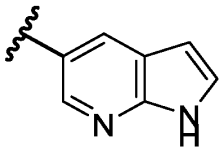
isoquinolinyl, substituted with NH_2 at the 1- position  , optionally further substituted with 1 or 2 substituents as for heteroaryl[a].

85. A compound of formula (I) according to numbered embodiment 68, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein B is azaindole, optionally substituted as for heteroaryl[a].

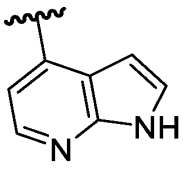
86. A compound of formula (I) according to numbered embodiment 85, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein B is azaindole, selected from  ,  and  , optionally substituted as for heteroaryl[a].

87. A compound of formula (I) according to numbered embodiment 85, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein B is 7-azaindole, optionally substituted as for heteroaryl[a].

88. A compound of formula (I) according to numbered embodiment 87, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

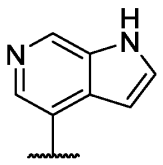
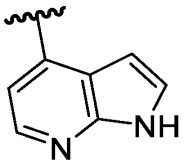
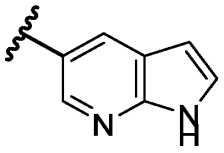
wherein B is 7-azaindole, selected from  and  , optionally substituted as for heteroaryl[a].

89. A compound of formula (I) according to numbered embodiment 87, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

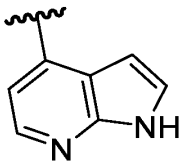
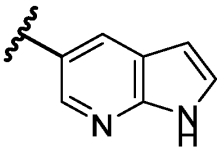
wherein B is 7-azaindole  , optionally substituted as for heteroaryl[a].

90. A compound of formula (I) according to numbered embodiment 87, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein B is 7-azaindole substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

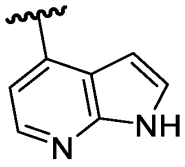
91. A compound of formula (I) according to numbered embodiment 85, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein B is azaindole, selected from  ,  and  , substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

92. A compound of formula (I) according to numbered embodiment 87, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

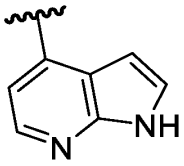
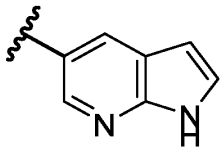
wherein B is 7-azaindole, selected from  and  , substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

93. A compound of formula (I) according to numbered embodiment 87, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

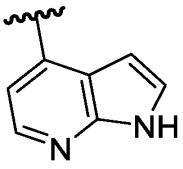
wherein B is 7-azaindole  substituted with methyl, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

94. A compound of formula (I) according to numbered embodiment 87, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein B is 7-azaindole substituted with chloro, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

95. A compound of formula (I) according to numbered embodiment 87, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein B is 7-azaindole, B can be selected from  or  , substituted with chloro, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

96. A compound of formula (I) according to numbered embodiment 87, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein B is 7-azaindole  substituted with chloro, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

97. A compound of formula (I) according to any of numbered embodiments 62 to 87, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein B is substituted with NH_2, and optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

98. A compound of formula (I) according to any of numbered embodiments 66 to 97, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein B is substituted with halo, and, where possible, optionally substituted with 1 or 2 further substituents as for heteroaryl[a].

99. A compound of formula (I) according to numbered embodiment 98, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof, wherein the halo is Cl.

100. A compound of formula (I) according to any preceding numbered embodiment, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein AW- is selected from -(CHR12)-A, $-(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A, $-(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A, $-(CH_2)_{0-6}$-NH-$(CH_2)_{0-6}$-A, $-(CH_2)_{0-3}$-(phenyl)-$(CH_2)_{0-3}$-A and $-(CH_2)_{0-6}$-NH-C(=O)-$(CH_2)_{0-6}$-A.

101. A compound of formula (I) according to any preceding numbered embodiment, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein AW- is selected from -(CHR12)-A, $-(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A, and $-(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A.

102. A compound of formula (I) according to any preceding numbered embodiment, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein AW- is $-(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A.

103. A compound of formula (I) according to any preceding numbered embodiment, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein AW- is $-CH_2$-O-A.

104. A compound of formula (I) according to numbered embodiment 101, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein AW- is selected from -(CHR12)-A, and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A.

105. A compound of formula (I) according to numbered embodiment 104, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein AW- is -(CHR12)-A.

106. A compound of formula (I) according to numbered embodiment 105, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein -(CHR12)-A is -(CH_2)-A.

107. A compound of formula (I) according to numbered embodiment 104, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein AW- is -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A.

108. A compound of formula (I) according to numbered embodiment 107, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein AW- is -(CH_2)-O-$(CH_2)_{0-6}$-A.

109. A compound of formula (I) according to numbered embodiment 107, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein AW- is -$(CH_2)_{0-6}$-O-A.

110. A compound of formula (I) according to any of numbered embodiments 104 or 107 to 58, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic

and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein AW- is -(CH_2)-O-A.

111. A compound of formula (I) according to numbered embodiment 107, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein AW- is -$(CH_2)_{0-6}$-O-(CH_2) -A.

112. A compound of formula (I) according to numbered embodiment 107, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

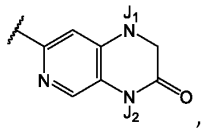
wherein AW- is -O-$(CH_2)_{0-6}$-A.

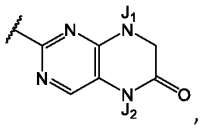
113. A compound of formula (I) according to any of numbered embodiments 104, 107 or 110 to 111, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein AW- is -O-(CH_2)-A.

114. A compound of formula (I) according to any preceding numbered embodiment or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein A is not:

(iii)  , which may be optionally substituted at J_1, J_2, or any other ring position on A; or

(iv)  , which may be optionally substituted at J_1, J_2, or any other ring position on A.

115. A compound of formula (I) according to any preceding numbered embodiment or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein A is a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN;

wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro.

116. A compound of formula (I) according to numbered embodiment 115 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein A is a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN;

wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro.

117. A compound of formula (I) according to numbered embodiment 116 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein A is a 9 or 10 membered bicyclic ring system containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected

from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN;

wherein at least one of the rings forming the bicyclic ring system is aromatic.

118. A compound of formula (I) according to numbered embodiment 117 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein A is a 9 or 10 membered bicyclic ring system containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN;

wherein both of the rings forming the bicyclic ring system are aromatic.

119. A compound of formula (I) according to any of numbered embodiments 117 to 118, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein A is a 9 membered bicyclic ring.

120. A compound of formula (I) according to numbered embodiment 116, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein A is a 6 or 7 membered mono- or bi- cyclic ring system, containing one N ring member and optionally one or two further ring members independently selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN;

wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro.

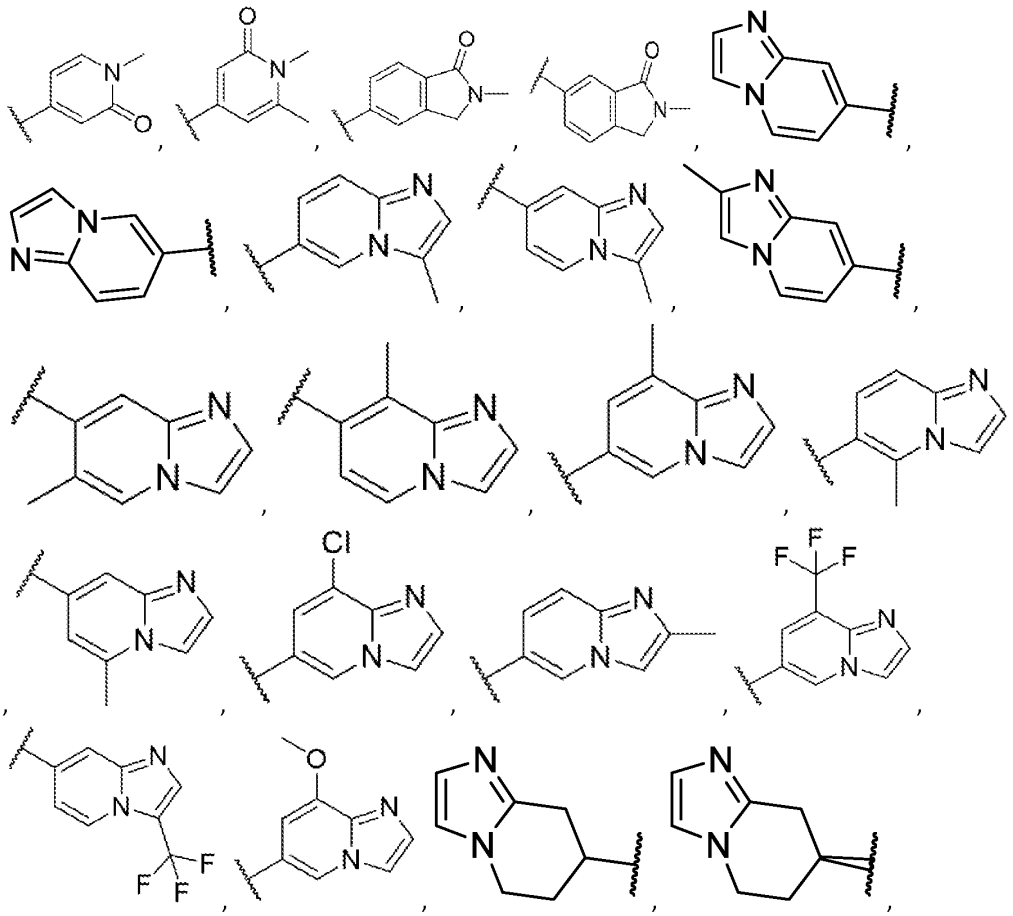
121. A compound of formula (I) according to numbered embodiment 120, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic

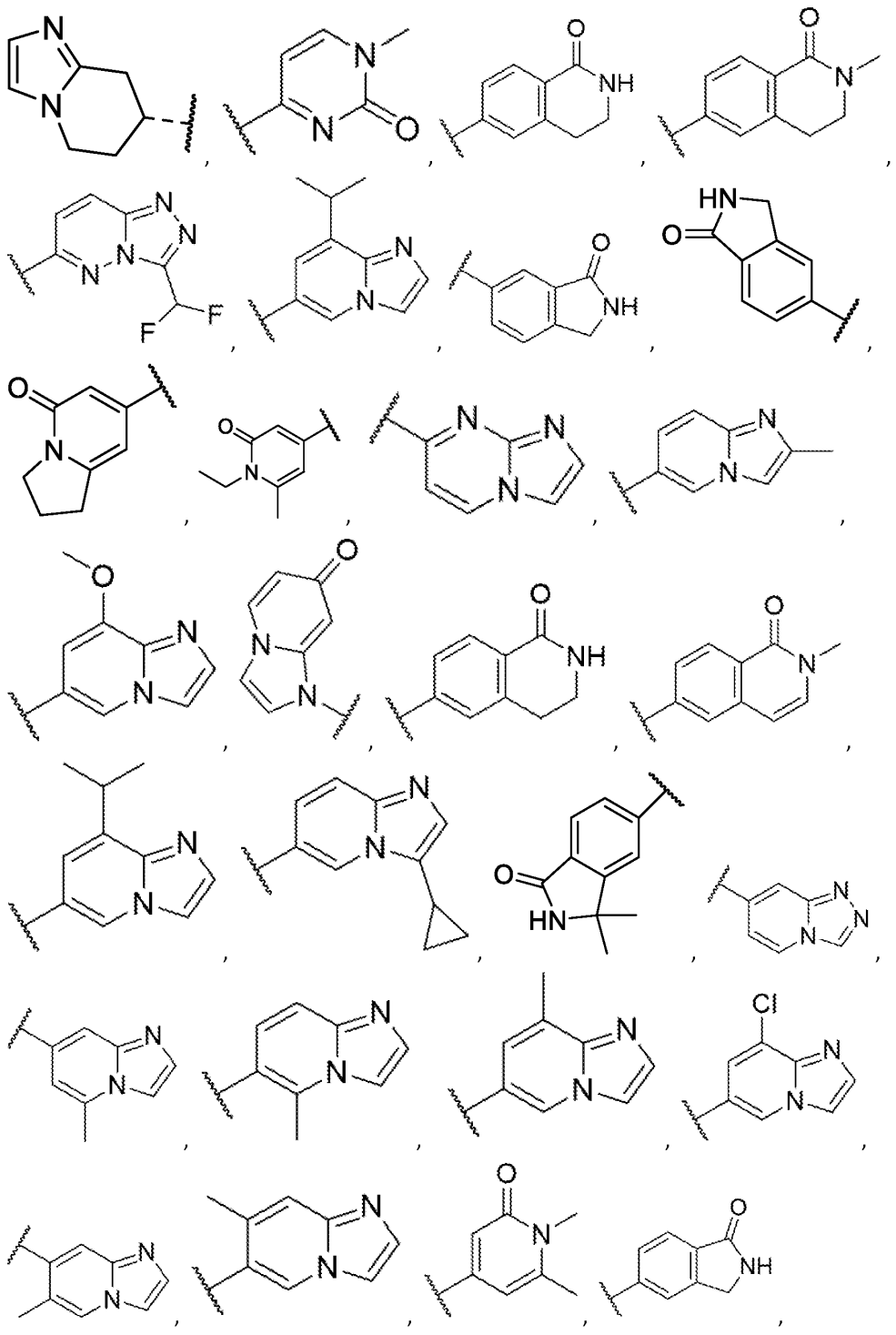
mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

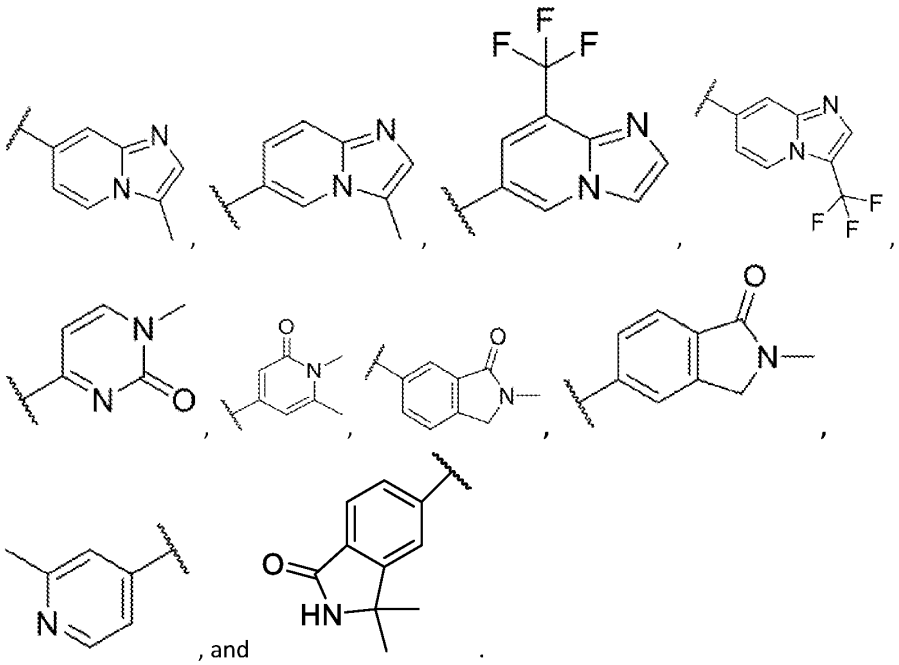
wherein A is a 6 membered monocyclic ring system containing one N ring member and optionally one further ring member selected from N and O, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN.

122. A compound of formula (I) according to numbered embodiment 115 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein A is selected from:

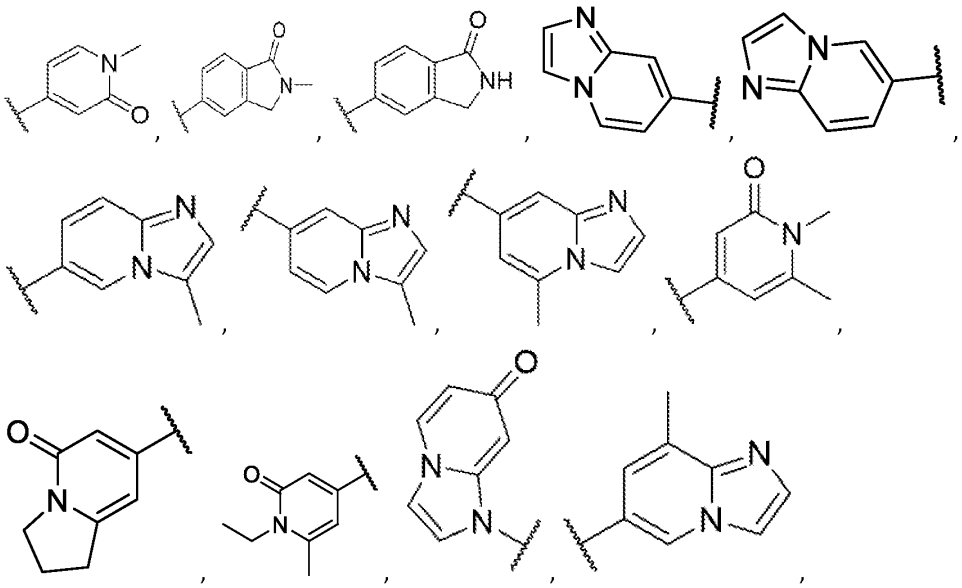


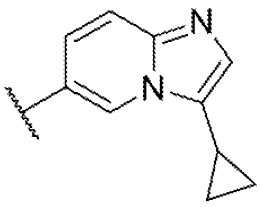
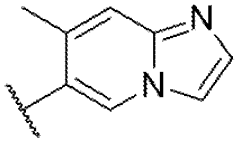
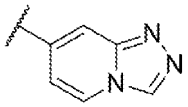
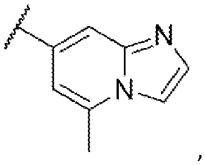
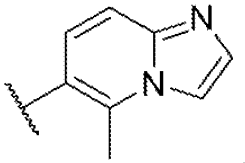
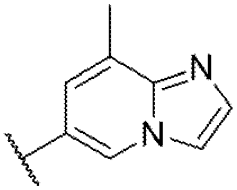
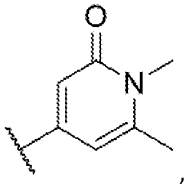
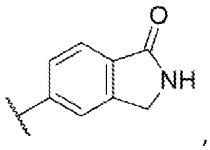
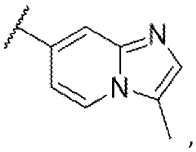
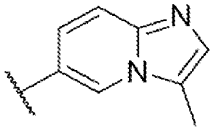
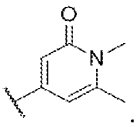




123. A compound of formula (I) according to numbered embodiment 115 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

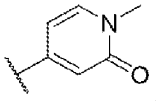
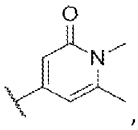
wherein A is selected from:




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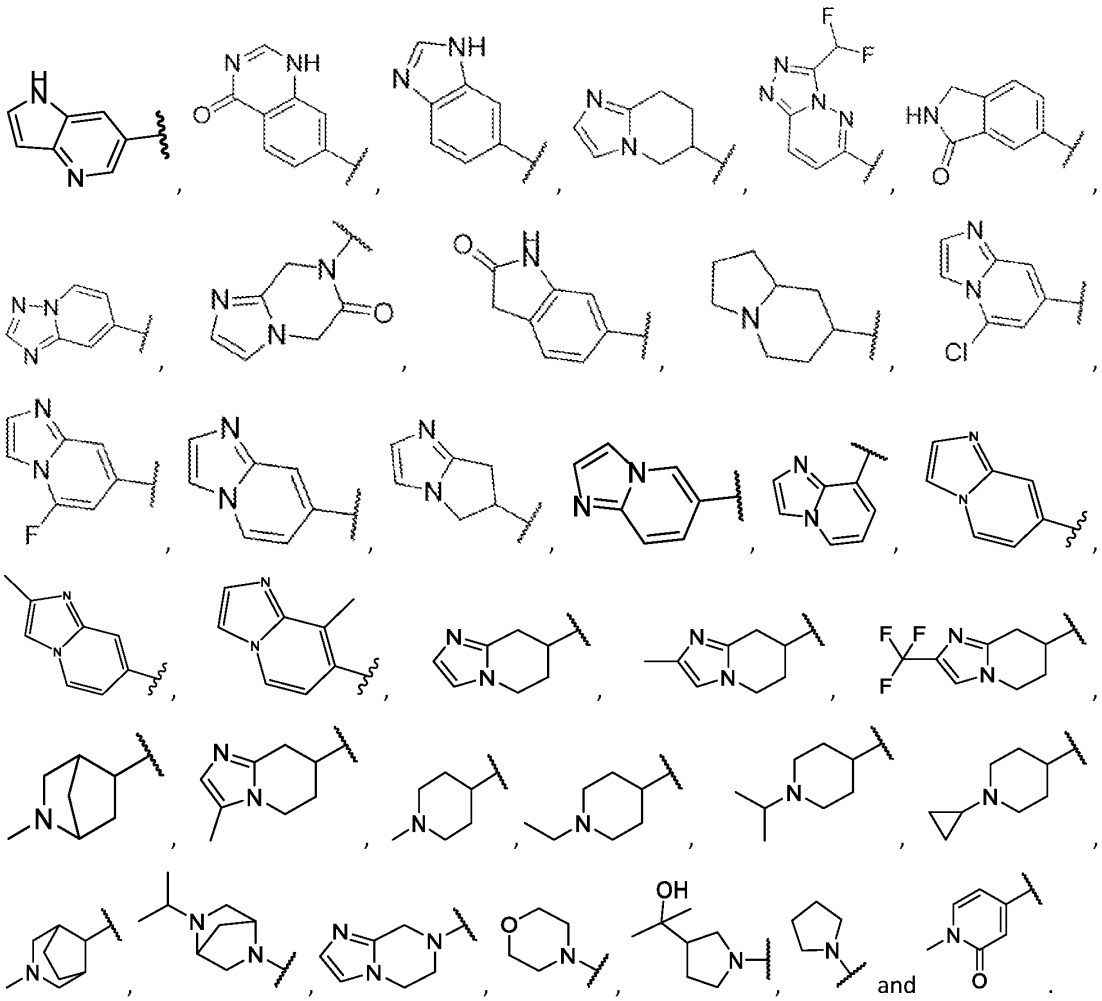
124. A compound of formula (I) according to numbered embodiment 115 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein A is selected from:


, and

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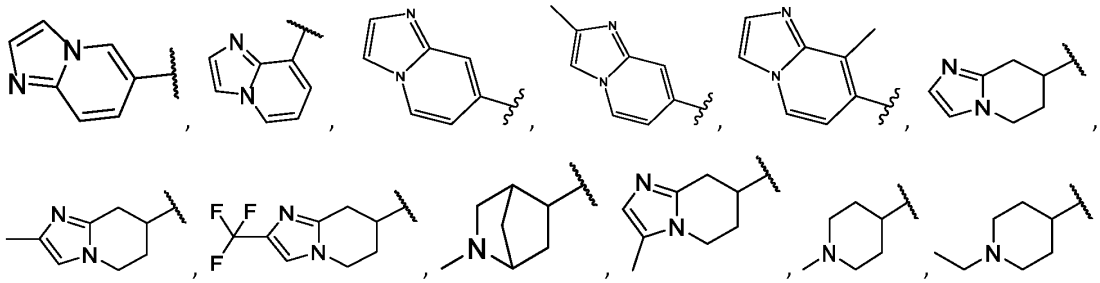
125. A compound of formula (I) according to numbered embodiment 116 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

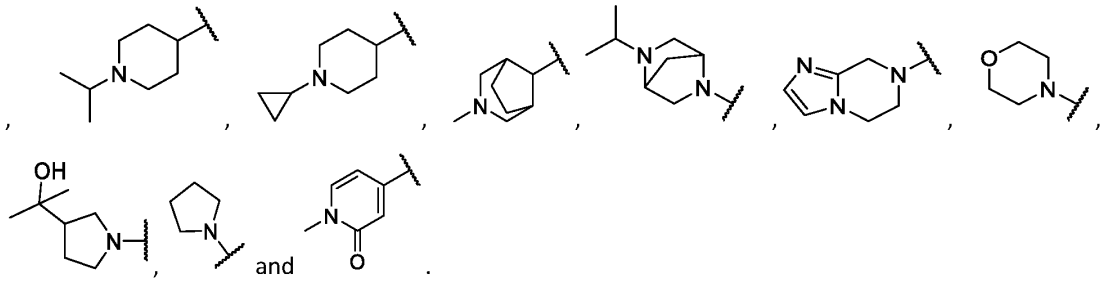
wherein A is selected from:



126. A compound of formula (I) according to numbered embodiment 125 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

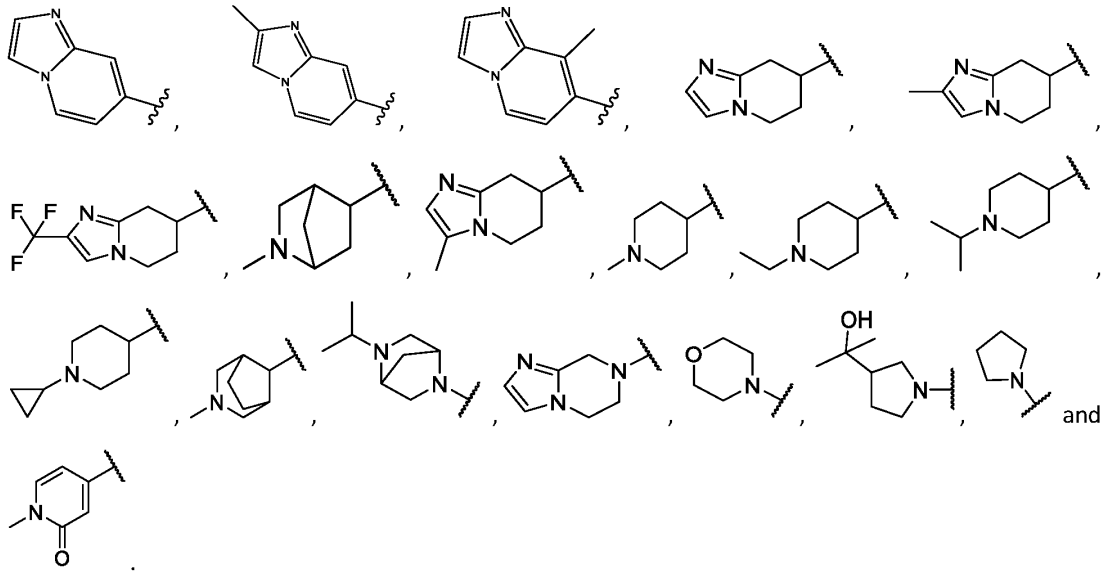
wherein A is selected from:





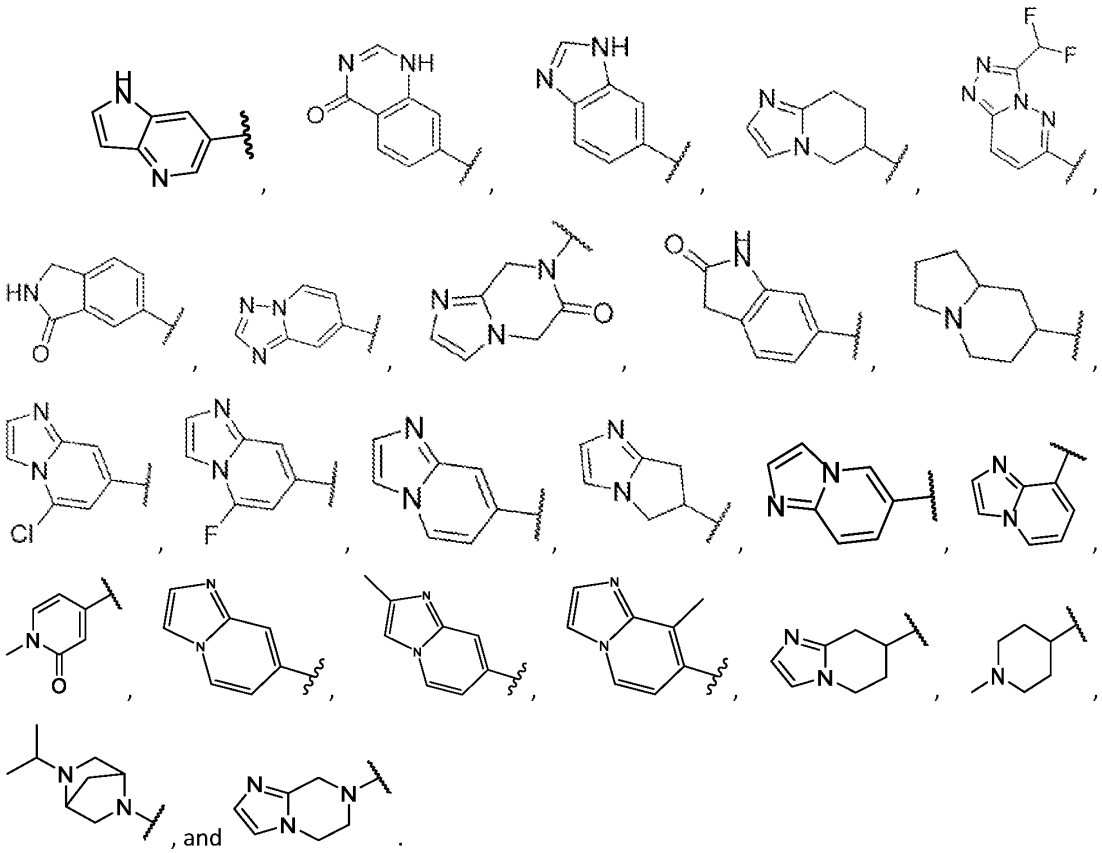
127. A compound of formula (I) according to numbered embodiment 126 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein A is selected from:



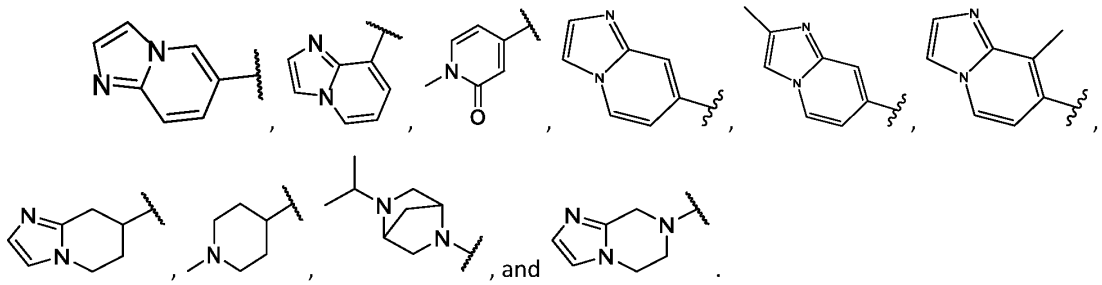
128. A compound of formula (I) according to numbered embodiment 116 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein A is selected from:



129. A compound of formula (I) according to numbered embodiment 128 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

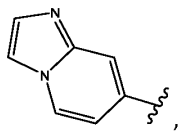
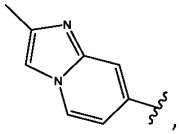
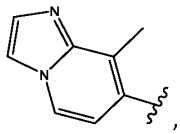
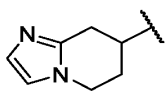
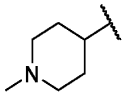
wherein A is selected from:

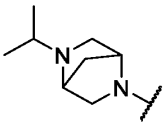
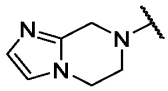


130. A compound of formula (I) according to numbered embodiment 129 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic

mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

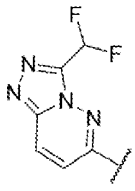
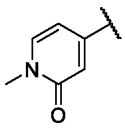
wherein A is selected from:

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 , and  .

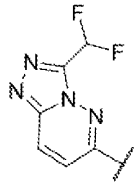
131. A compound of formula (I) according to numbered embodiment 125 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein A is selected from:

 and  .

132. A compound of formula (I) according to numbered embodiment 131 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

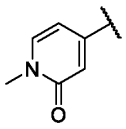
wherein A is:

 .

133. A compound of formula (I) according to numbered embodiment 131 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic

mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein A is:



.

134. A compound selected from Table 1a, Table 1b, Table 2a, Table 2b, Table 3a, Table 4a, Table 5b, Table 6a, Table 6b, Table 7a, Table 7b, Table 8a, Table 8b, Table 9b, Table 10a, Table 10b, Table 11b, Table 12b, or Table 13b, or a pharmaceutically acceptable salt, solvate, or solvate of a salt thereof.

135. A compound selected from Table 1a, Table 2a, Table 3a, Table 4a, Table 6a, Table 7a, Table 8a, or Table 10a, or a pharmaceutically acceptable salt, solvate, or solvate of a salt thereof.

136. A compound selected from Example numbers 1001, 1002, 1002.1, 1002.2, 1003, 1004, 1005, 1005.1, 1005.2, 1006, 1007, 1008, 1009, 1010, 1011, 1012, 1013, 1014, 1015, 1016, 1017, 1018, 1019, 2020, 2021, 2022, 3023 or 3024, or a pharmaceutically acceptable salt, solvate, or solvate of a salt thereof.

137. A compound selected from Example numbers 1001, 1002, 1002.1, 1002.2, 1003, 1004, 1005, 1005.1, 1005.2, 1006, 1007, 1008, 1009, 1010 or 1011, or a pharmaceutically acceptable salt, solvate, or solvate of a salt thereof.

138. A pharmaceutical composition comprising: a compound, or a pharmaceutically acceptable salt and/or solvate thereof, according to any of numbered embodiments 1 to 137, and at least one pharmaceutically acceptable excipient.

139. A compound, or a pharmaceutically acceptable salt and/or solvate thereof, as defined in any of numbered embodiments 1 to 137, or the pharmaceutical composition according to numbered embodiment 138, for use in medicine.

140. A compound, or a pharmaceutically acceptable salt and/or solvate thereof, as defined in any of numbered embodiments 1 to 137, or the pharmaceutical composition according to

numbered embodiment 138, for use in a method of treatment of a disease or condition in which Factor XIIa activity is implicated.

141. A compound, a pharmaceutically acceptable salt and/or solvate thereof, or a pharmaceutical composition for use as defined in numbered embodiment 140, wherein the disease or condition in which Factor XIIa activity is implicated is a bradykinin-mediated angioedema, wherein the bradykinin-mediated angioedema is hereditary angioedema.

142. A compound, a pharmaceutically acceptable salt and/or solvate thereof, or a pharmaceutical composition for use as defined in numbered embodiment 140, wherein the disease or condition in which Factor XIIa activity is implicated is a bradykinin-mediated angioedema, wherein the bradykinin-mediated angioedema is non hereditary.

143. A compound, a pharmaceutically acceptable salt and/or solvate thereof, or a pharmaceutical composition for use as defined in numbered embodiment 140, wherein the disease or condition in which Factor XIIa activity is implicated is selected from vascular hyperpermeability, stroke including ischemic stroke and haemorrhagic accidents; retinal edema; diabetic retinopathy; impaired visual acuity; DME; retinal vein occlusion; and AMD.

144. A compound, a pharmaceutically acceptable salt and/or solvate thereof, or a pharmaceutical composition for use as defined in numbered embodiment 140 wherein the disease or condition in which Factor XIIa activity is implicated is a thrombotic disorder.

145. A compound, a pharmaceutically acceptable salt and/or solvate thereof, or a pharmaceutical composition for use as defined in numbered embodiment 144, wherein the thrombotic disorder is thrombosis; thromboembolism caused by increased propensity of medical devices that come into contact with blood to clot blood; prothrombotic conditions such as disseminated intravascular coagulation (DIC), Venous thromboembolism (VTE), cancer associated thrombosis, complications caused by mechanical and bioprosthetic heart valves, complications caused by catheters, complications caused by ECMO, complications caused by LVAD, complications caused by dialysis, complications caused by CPB, sickle cell disease, joint arthroplasty, thrombosis induced to tPA, Paget-Schroetter syndrome and Budd-Chari syndrome; atherosclerosis; COVID-19; acute respiratory distress syndrome (ARDS); idiopathic pulmonary fibrosis (IPF); rheumatoid arthritis (RA); and cold-induced urticarial autoinflammatory syndrome.

146. A compound, a pharmaceutically acceptable salt and/or solvate thereof, or a pharmaceutical composition for use as defined in numbered embodiment 144, wherein the disease or condition in which Factor XIIa activity is implicated is neuroinflammation; neuroinflammatory/neurodegenerative disorders such as MS (multiple sclerosis); other neurodegenerative diseases such as Alzheimer's disease, epilepsy and migraine; sepsis; bacterial sepsis; inflammation; vascular hyperpermeability; and anaphylaxis.

147. A compound, a pharmaceutically acceptable salt and/or solvate thereof, or a pharmaceutical composition for use as defined in numbered embodiment 140, wherein the disease or condition in which Factor XIIa activity is implicated is obesity or diabetes.

Synthetic Methods

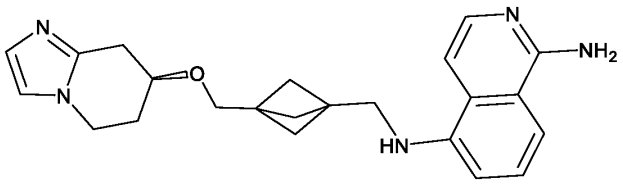
The compounds of the present invention can be prepared according to the procedures of the following schemes and examples, using appropriate materials, and are further exemplified by the specific examples provided herein below. Moreover, by utilising the procedures described herein, one of ordinary skill in the art can readily prepare additional compounds that fall within the scope of the present invention claimed herein. The compounds illustrated in the examples are not, however, to be construed as forming the only genus that is considered as the invention. Those skilled in the art will readily understand that known variations of the conditions, processes and order in which the synthetic steps are performed in the following preparative procedures can be used to prepare these compounds.

The compounds and intermediates of the invention may be isolated in the form of their pharmaceutically acceptable salts, such as those described previously herein above. The interconversion between free form and salt form would be readily known to those skilled in the art.

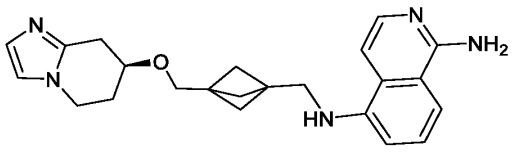
It may be necessary to protect reactive functional groups (e.g. hydroxy, amino, thio or carboxy) in intermediates used in the preparation of compounds of the invention to avoid their unwanted participation in a reaction leading to the formation of the compounds. Conventional protecting groups, for example those described by T. W. Greene and P. G. M. Wuts in "Protective groups in organic chemistry" John Wiley and Sons, 4th Edition, 2006, may be used. For example, a common amino protecting group suitable for use herein is tert-butoxy carbonyl (boc), which is readily removed by treatment with an acid such as trifluoroacetic acid or hydrogen chloride in an organic solvent such as dichloromethane. Alternatively the amino protecting group may be a benzyloxycarbonyl (Cbz or Z) group which can be removed by hydrogenation with a palladium catalyst under a hydrogen atmosphere or 9-fluorenylmethyloxycarbonyl (Fmoc) group which can be removed by solutions of secondary organic amines such as diethylamine or piperidine in an organic solvent. Carboxyl groups are typically protected as esters such as methyl, ethyl, benzyl or tert-butyl which can all be removed by hydrolysis in the presence of bases such as lithium or sodium hydroxide. Benzyl protecting groups can also be removed by hydrogenation with a palladium catalyst under a hydrogen atmosphere whilst tert-butyl groups can also be removed by trifluoroacetic acid. Alternatively a trichloroethyl ester protecting group is removed with zinc in acetic acid. A common hydroxy protecting group suitable for use herein is a methyl ether, deprotection conditions comprise refluxing in 48% aqueous HBr, or by stirring with borane tribromide in an organic solvent such as DCM. Alternatively where a hydroxy group is protected as a benzyl ether, deprotection conditions comprise hydrogenation with a palladium catalyst under a hydrogen atmosphere.

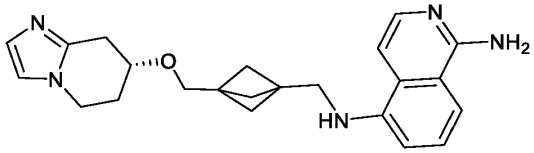
The graphic representations of racemic, ambiscalemic and scalemic or enantiomerically pure compounds used herein are taken from Maehr *J. Chem. Ed.* 62, 114-120 (1985): solid wedges ( ) and broken wedges ( ) are used to denote the absolute configuration of a chiral element; wavy lines ( ) indicate disavowal of any stereochemical implication which the bond it represents could generate; solid bold lines ( ) and broken bold lines ( ) are geometric descriptors indicating the relative configuration shown, but denoting racemic character; and wedge outlines ( ) and broken lines ( ) denote enantiomerically pure compounds of indeterminate absolute configuration. For nomenclature in the text corresponding to wedge outlines ( ) and broken lines ( ), we define R* and S* as indicating single enantiomers of uncertain absolute configuration. Additionally for nomenclature in the text corresponding to wedge outlines ( ) and broken lines ( ) which results in cis and trans isomers about a constrained ring system, we define cis* and trans* as indicating isomers of uncertain configuration.

Thus, for example, in examples 1002.1 and 1002.2 below, the synthesis of (S*)-N5-((3-(((5,6,7,8-tetrahydroimidazo[1,2-a]pyridin-7-yl)oxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine and (R*)-N5-((3-(((5,6,7,8-tetrahydroimidazo[1,2-a]pyridin-7-yl)oxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine are described. The (R*) and (S*) are intended to indicate that the product is a single enantiomer possessing the characteristics described (eq. NMR, HPLC, retention time etc), in which each of the chiral centres is believed on the basis of circumstantial evidence to be of the configuration shown, but the absolute configuration has not been confirmed. Thus, for example compound 1002.1, the depiction:

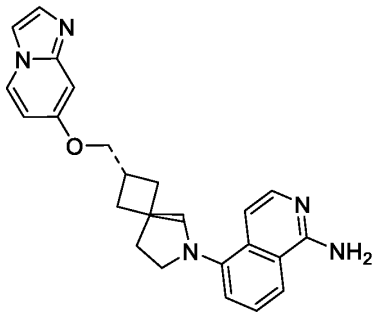


means that the compound is a single one of the following two stereoisomers, and probably the first:

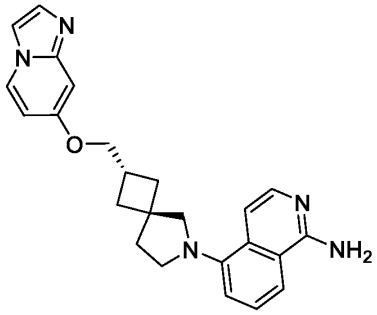


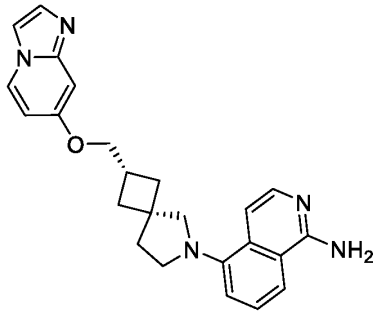


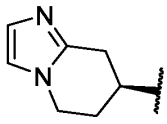
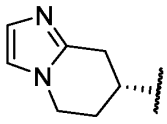
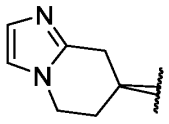
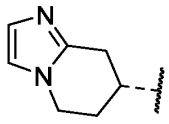
Additionally, for example, in examples 8806 and 8807 below, the synthesis of 5-(trans*-2-((imidazo[1,2-a]pyridin-7-yloxy)methyl)-6-azaspiro[3.4]octan-6-yl)isoquinolin-1-amine and 5-(cis*-2-((imidazo[1,2-a]pyridin-7-yloxy)methyl)-6-azaspiro[3.4]octan-6-yl)isoquinolin-1-amine are described. The trans* and cis* are intended to indicate that the product is a single isomer possessing the characteristics described (eq. NMR, HPLC, retention time etc), in which each of the combination of the chiral centres is believed on the basis of circumstantial evidence to be of the configuration shown, but the configuration has not been confirmed. Thus, for example compound 8806, the depiction:

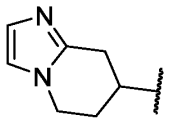


means that the compound is a single one of the following two isomers, and probably the first:





As used herein, a depiction including wedges or broken lines (eg.  ,  ,  , or ) indicates that the structure encompasses purity of that relative or absolute configuration of at least 80% ee, preferably >90% ee.

As used herein, when a compound possesses a centre of asymmetry, its depiction with simple lines (eg. ) indicates that the structure includes any and all stereoisomers, without regard to enantiomeric purity.

The invention is illustrated by the following non-limiting examples in which the following abbreviations and definitions are used:

AcOH	acetic acid
aq	aqueous solution
AIBN	azobisisobutyronitrile
boc	tert-butoxy carbonyl
Boc_2O	di-tert-butyl dicarbonate
BrettPhos Pd G3	[(2-di-cyclohexylphosphino-3,6-dimethoxy-2′,4′,6′- triisopropyl-1,1′-biphenyl)-2-(2′-amino-1,1′ -biphenyl)]palladium(II) methanesulfonate
BrettPhos Pd G4	(SP-4-3)-[dicyclohexyl[3,6-dimethoxy-2′,4′,6′-tris(1-methylethyl)[1,1′-biphenyl]-2-yl]phosphine-κP](methanesulfonato-κO)[2′-(methylamino-κN)[1,1′-biphenyl]-2-yl-κC]palladium (CAS no. 1599466-83-7)
tBu	tert-butyl
tert-BuBrettphos Pd G3	[(2-di-tert-butylphosphino-3,6-dimethoxy-2′,4′,6′-triisopropyl-1,1′-biphenyl)-2-(2′-amino-1,1′-biphenyl)]palladium(II) methanesulfonate
Cbz	benzyl carbamate
CDI	1,1′-carbonyldiimidazole
Celite®	Filter agent (diatomaceous earth)
DCM	dichloromethane
DIAD	diisopropyl azodicarboxylate
DIPEA	N,N-diisopropylethylamine
DMF	N,N-dimethylformamide
DMSO	dimethyl sulfoxide
EDC	1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride
eq	equivalent
Et_2O	diethyl ether
Et	ethyl

EtOH	ethanol
EtOAc	ethyl acetate
HATU	2-(3H-[1,2,3]triazolo[4,5-b]pyridin-3-yl)-1,1,3,3-tetramethylisouronium hexafluorophosphate(V)
h	Hours
HOBt	1-hydroxybenzotriazole hydrate
IPA	isopropyl alcohol
LCMS	Liquid chromatography mass spectrometry
LiHMDS	lithium hexamethyldisilazide
Me	methyl
MeCN	acetonitrile
MeOH	methanol
min	minutes
MS	mass spectrum
Ms	methanesulfonyl
MsCl	methanesulfonyl chloride
NBS	*N*-bromosuccinimide
NCS	*N*-chlorosuccinimide
NMR	nuclear magnetic resonance spectrum
NMP	N-methyl-2-pyrrolidone
OAc	acetate
Pet. Ether	petroleum ether fraction boiling at 60-80°C
Ph	phenyl
iPr	iso-propyl
nPr	n-propyl
RockPhos Pd G3	[(2-di-tert-butylphosphino-3-methoxy-6-methyl-2′,4′,6′-triisopropyl-1,1′-biphenyl)-2-(2-aminobiphenyl)]palladium(II) methanesulfonate
RuPhos Pd G3	(2-dicyclohexylphosphino-2′,6′-diisopropoxy-1,1′-biphenyl)[2-(2′-amino-1,1′-biphenyl)]palladium(II) methanesulfonate
sat.	saturated
SCX	strong cation exchange cartridge
STAB	sodium triacetoxyborohydride
SWFI	sterile water for injection

rt	room temperature
TBAB	tetra-n-butylammonium bromide
TBAF	tetra-n-butylammonium fluoride
TBDMS	*tert*-butyldimethylsilyl
TBME	tert-butyl methyl ether
THF	tetrahydrofuran
TEA	triethylamine
TFA	trifluoroacetic acid
Z	benzyl carbamate

All reactions were carried out under an atmosphere of nitrogen unless specified otherwise.

Hydrogenations were typically carried out using an H-Cube® reactor (manufactured by Thalesnano, Inc, Hungary).

References to the use of microwave, a microwave reactor, microwave heating and microwave irradiation all refer to the use of a CEM Discover Microwave Reactor.

References to the use of a phase separator refer to columns fitted with a selectively permeable, optimized frit material that separates aqueous phase from an organic phase under gravity.

^{1}H NMR spectra were recorded using instrumentation selected from

- Bruker (500MHz or 400MHz) spectrometer with a Bruker Avance II or Avance III console
- Oxford (400 MHz) AS400 magnet with a Inova console

and reported as chemical shift (ppm). It will be understood that, where exchangeable protons are present in any compound, the number of protons in the ^{1}H NMR spectra may not exactly correspond to the number of protons in the structure of any compound synthesised herein.

Molecular ions were obtained using LCMS with appropriate conditions selected from

- Chromolith Speedrod RP-18e column, 50 x 4.6 mm, with a linear gradient 10% to 90% 0.1% HCO_2H/MeCN into 0.1% HCO_2H/H_2O over 13 min, flow rate 1.5 mL/min;
- Agilent, X-Select, acidic, 5-95% MeCN/water over 4 min. Data was collected using a Thermofinnigan Surveyor MSQ mass spectrometer with electrospray ionisation in conjunction with a Thermofinnigan Surveyor LC system;

- LCMS (Waters Acquity UPLC, C18, Waters X-Bridge UPLC C18, 1.7 µm, 2.1x30mm, Basic (0.1% Ammonium Bicarbonate) 3 min method;
- LCMS (Agilent, X-Select, Waters X-Select C18, 2.5 µm, 4.6x30 mm, Acidic 4 min method, 95-5 MeCN/water);
- LCMS (Agilent, Basic, Waters X-Bridge C18, 2.5 µm, 4.6x30 mm, Basic 4 min method, 5-95 MeCN/water;
- Acquity UPLC BEH C18 1.7 µM column, 50 x 2.1 mm, with a linear gradient 10% to 90% 0.1% HCO2H/MeCN into 0.1% HCO2H/H2O over 3 min, flow rate 1 mL/min. Data was collected using a Waters Acquity UPLC mass spectrometer with quadropole dalton, photodiode array and electrospray ionisation detectors;
- Agilent 1100 LC/MSD with Kinetex® 5 µm EVO C18 100 Å LC 50 x 4.6 mm and Gemini® 5 µm NX-C18 110 Å LC 50 x 4.6 mm columns. Acidic mobile phases used a linear gradient of 5-95% 10 mM aq. NH_4HCO_2/MeCN and basic mobile phases used a linear gradient of 5-95% 10 mM aq. NH_4HCO_3/MeCN. Samples were run over 3 minutes, using a flow rate of 2.2 mL/min, and a pressure range of 0-200 bar. Data was collected using a Waters 3100 Mass Detector with single high resolution quadrupole and photomultiplier detectors and High Performance ZsprayTM dual-orthoganal API sources for standard ESI, or multimode ESI/APCI/ESCi®.
- UPLC (CSH C18 Column, 130Å, 1.7 µm, 2.1 mm x 30 mm, 3 min method, 0.1% Formic acid, 2-100% MeCN/water)
- LCMS (Cortecs C18+, 90Å, 2.7 µm, 2.1 mm x 30 mm, 3 min method, 0.1% Formic acid, 5-100% MeCN/water)
- UPLC (BEH C18 Column, 130Å, 1.7 µm, 2.1 mm x 30 mm, 3 min method, 0.1% Ammonium Hydroxide, 2-100% MeCN/water)
- LCMS (Kinetex Evo C18, 130Å, 2.5 µm, 2.1 mm x 30 mm, 3 min method, 0.1% Ammonium Hydroxide, 5-100% MeCN/water)

Flash chromatography was typically carried out over 'silica' (silica gel for chromatography, 0.035 to 0.070 mm (220 to 440 mesh) (e.g. Merck silica gel 60)), and an applied pressure of nitrogen up to 10 p.s.i accelerated column elution. Alternatively, pre-prepared cartridges of silica gel were used, for example pre-packed SiliaSep™ columns from Silicycle or Sfär C18 D – Duo 100 Å 30 µm columns from Biotage. Typical conditions included, for example, flow rate range of 18-200 mL/min, with an applied pressure range of 0-225 PSI. Hexanes, EtOAc, DCM, MeOH, were used as mobile phases for normal-phase chromatography purifications. MeOH, MeCN, 10mM Ammonium Formate pH 4 in H_2O and 10mM Ammonium Bicarbonate pH 10 in H_2O buffers were used as mobile phases for reverse-phase

chromatography. It will be understood that alternative conditions (such as flow rate ranges, applied pressures, solvents and pH) may be used for flash chromatography in order to separate and purify compounds synthesised herein.

The term "prep HPLC" refers to reverse phase preparative HPLC purifications. Typical instrumentation and conditions included, for example, Agilent 1100/1200 Series Prep-HPLC with MWD/DAD & MSD using 5-100% acetonitrile/methanol with 10mM NH_4HCO_3 pH 10 in H_2O buffer as a basic mobile phase and 5-100% acetonitrile/methanol with 10mM NH_4HCO_2 pH 4 in H_2O, 0.1% TFA in H_2O, or HFBA Buffer in H_2O as an acidic mobile phase. It will be understood that alternative conditions (such as choice of column, flow rate ranges, solvents and pH) may be used for prep HPLC in order to separate and purify compounds synthesised herein.

The procedure of lyophilisation (or freeze drying) is generally well known in the art. Typically the substance is taken up in water, if necessary with the addition of a minimum amount of MeCN to aid dissolution, and frozen, typically by rapid cooling in a cold bath at -78 °C. The resulting frozen solid mixture is evaporated to dryness *in vacuo*.

The term "concentrated" refers to evaporation of solvent under reduced pressure using a rotary evaporator, heating where necessary.

All solvents and commercial reagents were used as received.

IUPAC chemical names were generated using automated software such as Dotmatics Studies Notebook or ChemDraw (PerkinElmer). Compounds produced by the methods below may be isolated in salt forms. However, compound naming used herein typically refers to the compound without any salt counter ion.

The example compounds described herein can be prepared using conventional synthetic methods for example, but not limited to, the routes outlined in the General Schemes below, using, for example, the General Methods below.

General Methods

1. General Method 1: (GM1): mesylation and chlorination

a. General Method 1a (GM1a): mesylation

A solution of alcohol (1.0 eq) in DCM (20 mL) was cooled in an ice/water bath and methane sulfonyl chloride (1.2 eq) was added dropwise followed by TEA (1.4 eq) maintaining cooling. The reaction was

stirred at rt for 2-18 h. The reaction was diluted with DCM and washed with water. The aqueous layer was extracted with DCM (3 x 25 mL) and the combined organics were washed with brine, dried (Na_2SO_4), filtered and concentrated. The crude product was purified by flash chromatography.

b. General Method 1b (GM1b): chlorination *via* a mesylate

Methane sulfonyl chloride (2.5 eq) (0.6 mL, 8.32 mmol) was added to a solution of TEA (2.8 eq) and alcohol (1.0 eq) in DCM (20 mL) while cooling in an ice/water bath. The reaction was stirred at rt for 18 h. The reaction was diluted with DCM and washed with sat. $NaHCO_3$ (aq). The aqueous layer was extracted with DCM (3 x 25 mL) and the combined organics were washed with brine, dried (Na_2SO_4), filtered and concentrated. The crude product was purified by flash chromatography.

c. General Method 1c (GM1c): chlorination via NCS

A solution of indole or azaindole (1.0 eq) in DCM was protected from light and treated with NCS (3.75 eq) at rt for 12 - 48 h. The mixture was treated with 1M HCl (aq) and the phases separated. The organic phase was washed with brine, dried (Na_2SO_4), filtered, concentrated and purified by flash chromatography.

2. General Method 2 (GM2): SN_2 alkylation (O and N)

a. General Method 2a: SN_2 alkylation: NaH

To a suspension of NaH (60% wt. on mineral oil) (1.1 eq) in DMF in an ice/water bath was added a solution of alcohol, pyrrole or indole (1.0 eq) in DMF dropwise over 2 min. The mixture was allowed to warm to rt for 5 min before cooling again in an ice/water bath and treating with a solution of the alkylhalide or mesylate (1.0 eq) in DMF over 2 min. The mixture was maintained in an ice/water bath for 1 h before being allowed to warm to rt, or heated at elevated temperature and stirred for 2-18 h. Sat. NH_4Cl (aq) (50 mL) or sat. $NaHCO_3$ (aq) was added and extracted with EtOAc (x 3). The organic phases were combined, dried ($MgSO_4$), filtered and concentrated. The crude product was purified by flash chromatography.

b. General Method 2b: SN_2 alkylation; Cs_2CO_3 or K_2CO_3

A solution of alkyl halide or mesylate (1-2 eq), amine (1.0 eq), and base such as K_2CO_3, or Cs_2CO_3 (2.5 eq), in a solvent such as DMF, DMSO or MeCN, was stirred at 80 °C for 2-18 h. MeOH (5 mL) was added and the mixture was diluted with water (50 mL). The product was extracted into EtOAc (2 x 50 mL) and washed with brine (50 mL). The organic layer was dried (Na_2SO_4), filtered and concentrated. The product was either used directly or purified by flash chromatography.

3. General Method 3 (GM3): Reduction

a. General Method 3a (GM3a): nitrile reduction; H-Cube® with Pd/C or Raney Ni cartridge

The nitrile was dissolved in a 0.5M NH_3/MeOH solution passed through an H-Cube® reactor (Pd/C or Raney Ni cartridge), typical conditions: 50 °C, 'full' hydrogen delivery mode (50 bar), flow rate: 1 mL/min. The reaction was concentrated to afford the product which was used without further purification.

b. General Method 3b (GM3b): nitrile, amide and ester reduction; $LiAlH_4$ in THF

To a solution of amide, nitrile, or ester (1.0 eq) in THF in an ice/water bath was added $LiAlH_4$ (2M in THF) (2.0 eq) dropwise and the reaction mixture was allowed to warm to rt then stirred for 4-18 h. The reaction mixture was cooled in an ice/water bath, treated portionwise with $Na_2SO_4.10H_2O$ (3.5 eq) and stirred for 30 min before being dried ($MgSO_4$), filtering and washing with THF (10 mL). The filtrate was concentrated to afford the crude product which was used without purification or purified by flash chromatography.

c. General Method 3c: borane-THF

A solution of nitrile (1.0 eq) in THF was cooled in an ice/water bath before borane (1M in THF, 2.0 eq) was added dropwise. The reaction was allowed to warm to rt then heated to 60 °C for 16-96 h. MeOH was added and heating continued at 60 °C for 24 h before cooling to rt and concentrating. The product was isolated and purified using one of the following methods:

i) The crude product was loaded onto an SCX in MeOH and washed with MeOH. The product was eluted with 7M NH_3 in MeOH and the eluent concentrated.

ii) The crude product was purified by flash chromatography

iii) Boc_2O (1.2 eq) was added to the crude reaction mixture and stirred overnight. The solvent was evaporated in vacuo. The product was taken up in DCM, washed with water and brine, dried (Na_2SO_4), filtered and concentrated. The boc-protected amine was either used without further purification or purified by flash chromatography

d. General Method 3d: $NiCl_2$

A solution of nitrile (1.0 eq), $NiCl_2.6H_2O$ (1.0 eq) and Boc_2O (3.0 eq) in MeOH was cooled in an ice/water bath and sodium borohydride ($NaBH_4$) (5.0 eq) added portionwise. The reaction was allowed to warm to rt and stirred for 18 h. Water was added and the reaction mixture filtered, washed with THF and concentrated. The crude product was purified by flash chromatography.

e. General Method 3e: hydrogenation; Pd/C

To a solution of nitrile (1.0 eq) in MeOH or EtOH under an inert atmosphere was added 10% Pd/C (0.1-0.2 eq). Additives such as HCl, sulfuric acid, or Boc_2O may optionally be added. The reaction was stirred under an atmosphere of H2 (g) for 2-72h. The catalyst was removed by filtration over Celite®, which was washed

with EtOH. The product was isolated following concentration of the filtrate and used directly or purified by flash chromatography.

f. General Method 3f: ring saturation reduction

A biaryl ring (1.0 eq) was dissolved in EtOH and subjected to hydrogenation in the H-Cube® at 70 °C, 50 bar, 1 mL/min using a 10% Pd/C CatCart, recirculating when necessary. The solvent was removed *in vacuo* to afford the product which was used without purification.

4. General Method 4 (GM4): Buchwald

A suspension of amine or alcohol (1.0 eq), aryl halide (1.1 eq) and a base such as Cs_2CO_3, NaOtBu (2.0 eq) or LiHMDS (2.0 eq) in a degassed solvent such as THF or 1,4-dioxane was purged with N_2 (g). A Buchwald palladium precatalyst, such as BrettPhos Pd G3, (0.11 eq) was added and the mixture degassed and purged with N_2 (g) for 5 min. The reaction was heated in a sealed vial at rt - 60˚C for 30 min – 3 days as required. The product was isolated and purified using one of the following methods:

i) The reaction was quenched with AcOH (2.0 eq) and concentrated. The crude was purified by an SCX eluting with NH_3 in MeOH followed by purification by flash chromatography or prep HPLC.

ii) The reaction was quenched with AcOH (2.0 eq), filtered through Celite®, washing with EtOAc and the filtrate concentrated. The crude product was purified by flash chromatography

iii) The reaction mixture was acidified with AcOH (2.0 eq) and stirred for 5 min, 1M NH_3 in MeOH was added and the reaction mixture was concentrated on to silica and purified by flash chromatography.

iv) The reaction mixture was dry loaded on to silica and purified by flash chromatography.

5. General Method 5 (GM5): boc deprotection; HCl or TFA

a. General Method 5a: boc deprotection; HCl/dioxane

A suspension of boc protected amine (1.0 eq) in 1,4-dioxane was treated with 4M HCl in dioxane (10.0 eq) was added and the reaction stirred at rt for 2-24 h. The product was isolated and purified using one of the following methods:

i) The reaction mixture was concentrated, optionally azeotroping with Et_2O or toluene to afford the product as a hydrochloride salt.

ii) The reaction mixture was concentrated and the product was converted to free base using a bicarbonate cartridge, PL-HCO_3 MP SPE (Agilent), loading in MeOH. The filtrate was concentrated and triturated with Et_2O to afford the product.

b. General Method 5b: boc deprotection; TFA

A mixture of boc protected amine (1.0 eq) in DCM was treated with TFA (10.0 eq) and stirred at rt for 2 h. The mixture was passed directly through an SCX and washed with MeOH. The product was eluted with a solution of 7M NH_3 in MeOH and concentrated. The crude product was purified by flash chromatography or prep HPLC.

6. General Method 6 (GM6): pyridone chlorination

Pyridone (1.0 eq) was suspended in phosphorus oxychloride (large excess) and heated at reflux for 4 h. The reaction mixture was evaporated then azeotroped with toluene (x 2). The residue was used immediately in the next step, taking care to exclude moisture.

7. General Method 7 (GM7): SNAr Alkylation (O and N)

a. General Method 7a (GM7a): SNAr O-alkylation using NaH

To a suspension of NaH (60% wt. on mineral oil) (1.04 eq) in DMF in an ice/water bath was added a solution of alcohol (1.02 eq) in DMF dropwise over 2 min. The mixture was allowed to warm to rt for 5 min before cooling again in an ice/water bath and treating with pyridyl halide or aryl halide (1.0 eq). The reaction mixture was maintained in an ice/water bath for 1 h then warmed to rt for 18 h. The reaction mixture was cooled in an ice/water bath and sat. Na2CO3 (aq) was added followed by water. This was extracted with EtOAc (x 3) and the organic phases were combined, washed with 1:1 water/brine and brine. The organic phase was dried (MgSO4), filtered and concentrated. The crude product was purified by flash chromatography.

b. General Method 7b (GM7b): SNAr O-alkylation using Cs_2CO_3

To a solution of alcohol (1.0 eq) and pyridyl halide (1.0 eq) in MeCN was added Cs_2CO_3 (2.0 eq) and the mixture was stirred in a sealed vial at 50 °C for 18-72 h. The product was isolated and purified using one of the following methods

i) The reaction mixture was cooled to rt and diluted with water (10 mL). The crude product was extracted into DCM, dried ($MgSO_4$), filtered and concentrated. The residue was purified by flash chromatography

ii) The reaction mixture was filtered through Celite® and the filtrate was concentrated to yield the crude product which was either used without further purification or purified by flash chromatography

iii) The crude reaction mixture was passed directly through an SCX in MeOH. The SCX was washed with MeOH and the product was eluted with 7M NH_3 in MeOH. The crude product was purified by flash chromatography.

c. General Method 7c (GM7c): SNAr O-alkylation using NaOtBu

A solution of alcohol (1.0 eq), aryl bromide (1.0 eq) and NaOtBu (3.0 eq) in NMP was stirred in the microwave at 140 °C for 4 h. The crude reaction mixture was loaded onto an SCX in MeOH and washed with MeOH and the product was eluted with 7M NH_3 in MeOH (50 mL). The product was concentrated and purified by flash chromatography or prep HPLC.

d. General Method 7d (GM7d): SNAr N-alkylation

Amine (1.0 eq) and halopyridine (1.0 eq) were dissolved in MeCN (3 mL). K_2CO_3 (3.0 eq) was added and the reaction was stirred at 60 - 120 °C for 60 - 90 min under thermal heating or microwave irradiation. The reaction was diluted with water and extracted with iso-propanol/CHCl3 (1:10) (x 3). The combined organics were washed with brine, dried ($MgSO_4$) and concentrated. The product was isolated and used directly or purified by flash chromatography.

8. General Method 8 (GM8): 2,4-dimethoxybenzyl deprotection

A solution of 2,4-dimethyoxybenzyl protected amine (1.0 eq) in TFA (10 eq.) was stirred at rt - 50 °C for 60 min. The reaction mixture was concentrated. The resulting residue was suspended in MeOH (2 mL) and loaded on to an SCX, which was flushed with MeOH (4 x 5 mL). The product was eluted with a solution of 1N NH_3 in MeOH (4 x 5 mL). The solvent was removed in vacuo. The crude product was either used without further purification or purified by flash chromatography or prep HPLC.

9. General Method 9 (GM9): carbamate protection

To a solution of aminopyridine (1.0 eq) and TEA (2.0 eq) in DCM (12 mL) in an ice/water bath was added methylchloroformate (3.0 eq) and the reaction was stirred at rt for 48 h. The reaction mixture was diluted with DCM and washed with water (20 mL). The aqueous was extracted with DCM (3 x 80 mL) and the combined organics dried (Na_2SO_4), filtered and concentrated. The crude product was triturated with EtOAc.

10. General Method 10 (GM10): carbamate deprotection

a. General Method 10a: KOH

A mixture of methyl carbamate (1 eq) and KOH (6 eq) in MeOH was stirred at 60 °C for 12-48 h. The product was isolated and purified using one of the following methods:

i) The reaction was quenched with AcOH (6.0 eq) and the mixture was left to stir for 5 min before being concentrated. The residue was passed directly through an SCX in MeOH. The SCX was washed with MeOH and the product was eluted with 7M NH_3 in MeOH and lyophilised.

ii) The reaction was quenched with AcOH (6.0 eq) and the mixture was left to stir for 5 min before being concentrated. The residue was passed directly through an SCX in MeOH. The SCX was washed with

MeOH and the product was eluted with 7M NH_3 in MeOH. The product was purified by flash chromatography or prep HPLC

iii) The reaction was quenched with AcOH (6.0 eq), concentrated, and purified by prep HPLC.

b. General Method 10b: LiOH

To a solution of methyl carbamate (1 eq) in THF/water (10:1) was added lithium hydroxide monohydrate (3-5 eq) and the reaction stirred at 60 °C for 18 h - 4 days. The mixture was cooled to rt and concentrated. The crude residue was purified via flash chromatography or prep HPLC

11. General Method 11: SEM deprotection

A mixture of TFA acid (10 eq) was added dropwise to a rapidly stirred solution of indole or azaindole (1.0 eq) in DCM. The mixture was stirred at rt for 18 h. The reaction mixture was passed directly through an SCX in MeOH. The SCX was washed with MeOH and the product was eluted with 2.5M NH_3 in MeOH and concentrated. The crude product was purified by flash chromatography or prep HPLC.

12. General Method 12: Alkylation and cyclisation

To a solution of the amino substituted heteroaryl (e.g. pyridine) (1 eq) in EtOH (3 mL) were added $NaHCO_3$ (2 eq) and the chloromethyl aldehyde or chloromethyl ketone as applicable (2 eq). The mixture was stirred for 20 h at 75 °C. The mixture was then cooled to rt, filtered through Celite washing with EtOAc (50 mL) and concentrated. The product was purified by flash chromatography.

13. General Method 13: Hydroxylation

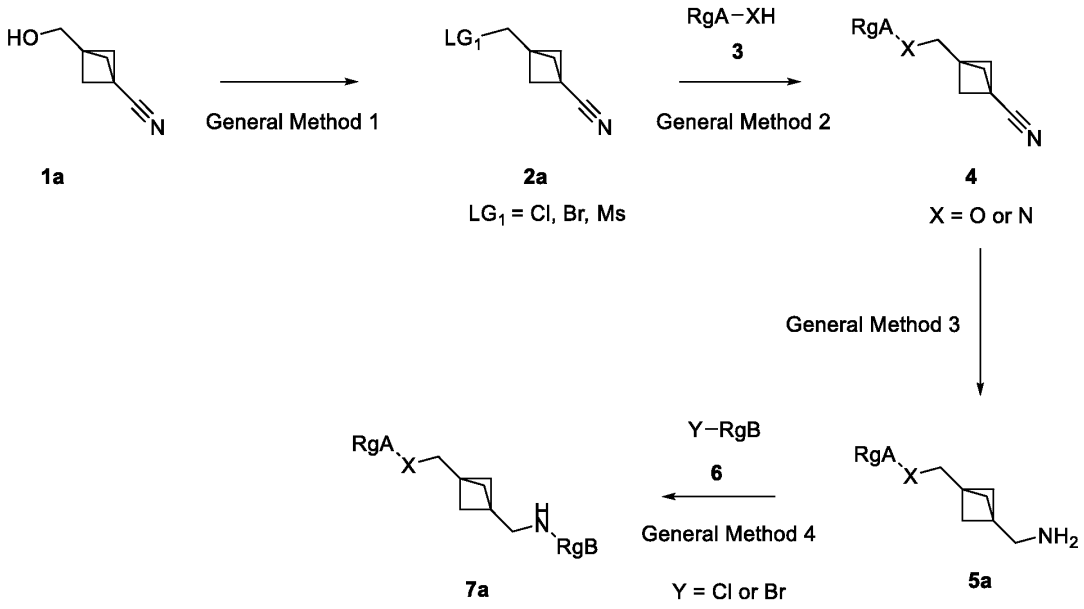
A solution of the aryl bromide or heteroaryl bromide (1.0 eq), bis(pinacolato)diboron (2.0 eq) and [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (0.1 eq) in anhydrous, degassed 1,4-dioxane was purged with N_2 (g) for 5 min. KOAc (3.0 eq) was added and the reaction stirred at 90 °C for 2 – 18 h. AcOH (2.0 eq) and water (1 mL) were added and the reaction stirred at rt for 15 min – 18 h. A solution of H_2O_2 in water (30% w/w, 2 eq) was added and the reaction mixture stirred for 1 – 18 h.

i) Typically for basic compounds: solid $Na_2S_2O_3$ was added and the reaction was stirred at rt for 5 min then diluted with EtOAc, filtered through Celite and concentrated. The residue was purified by SCX and flash chromatography.

ii) Typically for non basic compounds: sat. $Na_2S_2O_3$ (aq) and sat. $NaHCO_3$ (aq) were added and the aqueous was extracted with EtOAc. The combined organics were washed with brine, dried ($MgSO_4$), concentrated, and purified by flash chromatography

General Schemes

General Schemes 1-6 outline synthetic routes for certain example compounds and RgA, RgB, RgC and RgD refer to various substituents as required by the examples. For the sake of clarity General Schemes 1-6 are drawn with a bicyclopentyl central core group. Similar chemistry can be applied to examples with different core groups such as oxabicyclohexyl and oxabicycloheptyl.

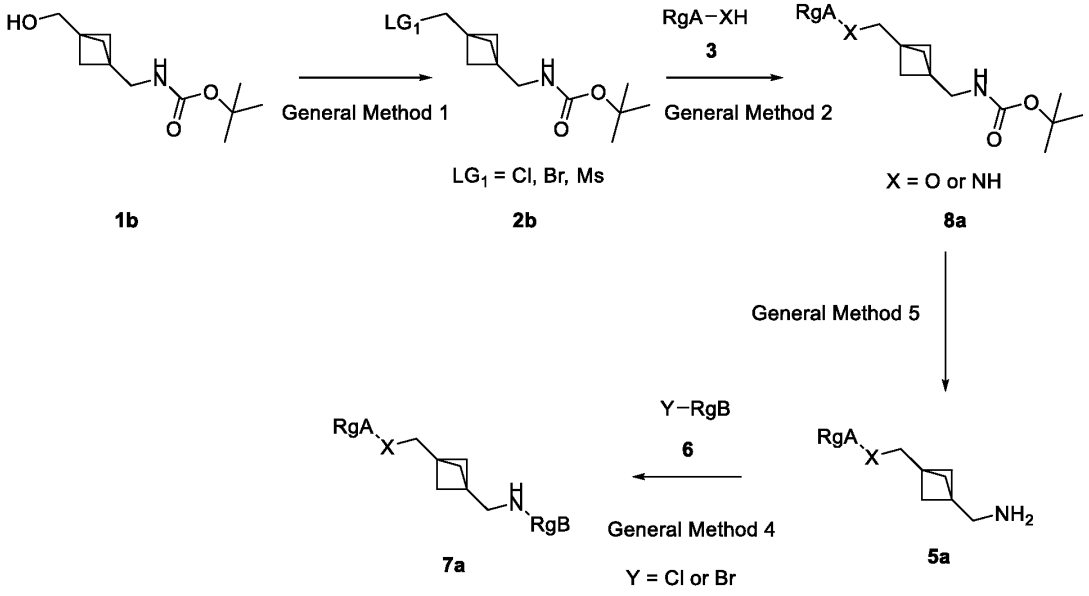


General Scheme 1

Alcohols such as **1a** are typically reacted to form a suitable leaving group, such as halide or mesylate and can be generated using conditions well known in the art such as, for example; chlorination *via* a mesylate, bromination with PBr_3, or bromination with CBr_4 and PPh_3, using a suitable solvent such as DCM, THF or CCl_4 (General Method 1), to give compound **2a**. Compound **2a** is subsequently reacted with an alcohol or amine **3** under typical alkylation conditions (General Method 2, eg KOtBu or NaH in DMF or Cs_2CO_3 or K_2CO_3 in MeCN or DMSO, with heating as necessary). The nitrile **4** can be reduced to amine **5a** under a variety of standard literature conditions well known in the art (General Method 3); for example under hydrogenation in the presence of Raney Ni, alternatively hydrogenation in the presence of Pd/C, or alternatively with $NiCl_2$ and sodium borohydride ($NaBH_4$) in the presence of Boc_2O, or alternatively with borane. The amine **5a** is reacted with aryl bromide or chloride **6** under Buchwald coupling conditions (General Method 4). This Buchwald coupling is carried out for example using a Buchwald pre catalyst, such as BrettPhos Pd G3 or BrettPhos Pd G4, in the presence of a base such a sodium tert-butoxide, caesium carbonate, or lithium hexamethyldisilazide (LiHMDS), in a solvent such as 1,4-dioxane or THF. The aryl bromide or chloride **6** can be prepared from readily available starting materials using methods known in

the art, or as described herein. Depending on the identity of RgB, a deprotection step (detailed above) may be required to obtain the example compound.

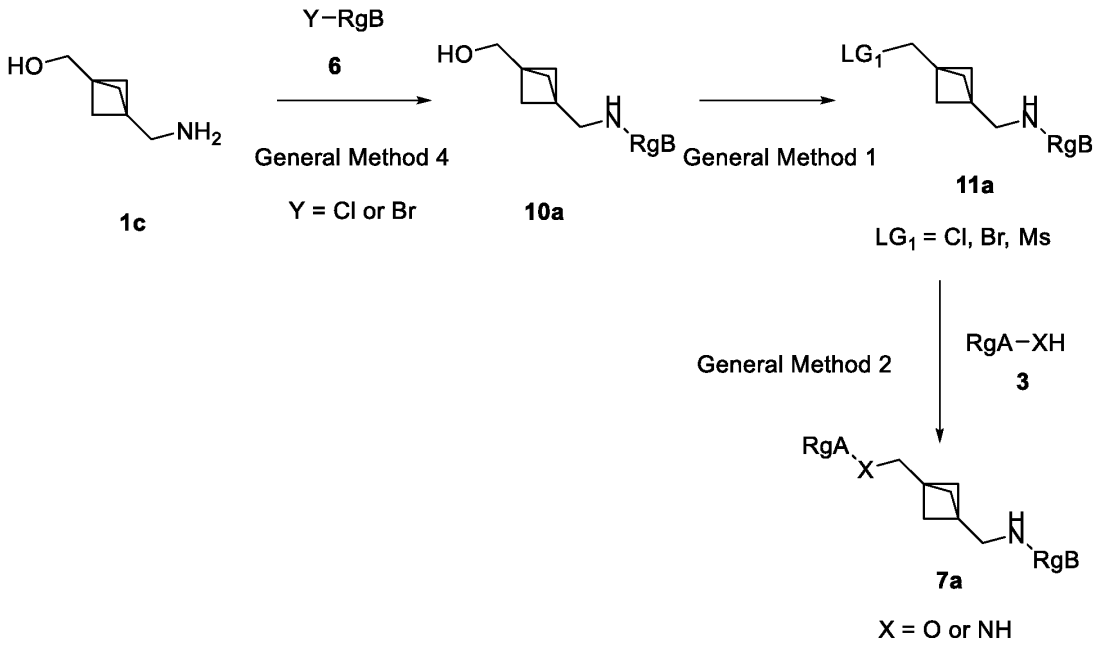
Alternatively, for example as shown in General Scheme 2, where material is available with the protected amine, for example compound **1b**, a similar synthetic sequence can be applied.



General Scheme 2

Following formation of a leaving group and alkylation**,** the *tert*-butoxy carbamate protecting group is removed from compound **8a** using standard conditions such as TFA, or HCl in 1,4-dioxane (General Method 5). Finally, Buchwald coupling (General Method 4) completes the route.

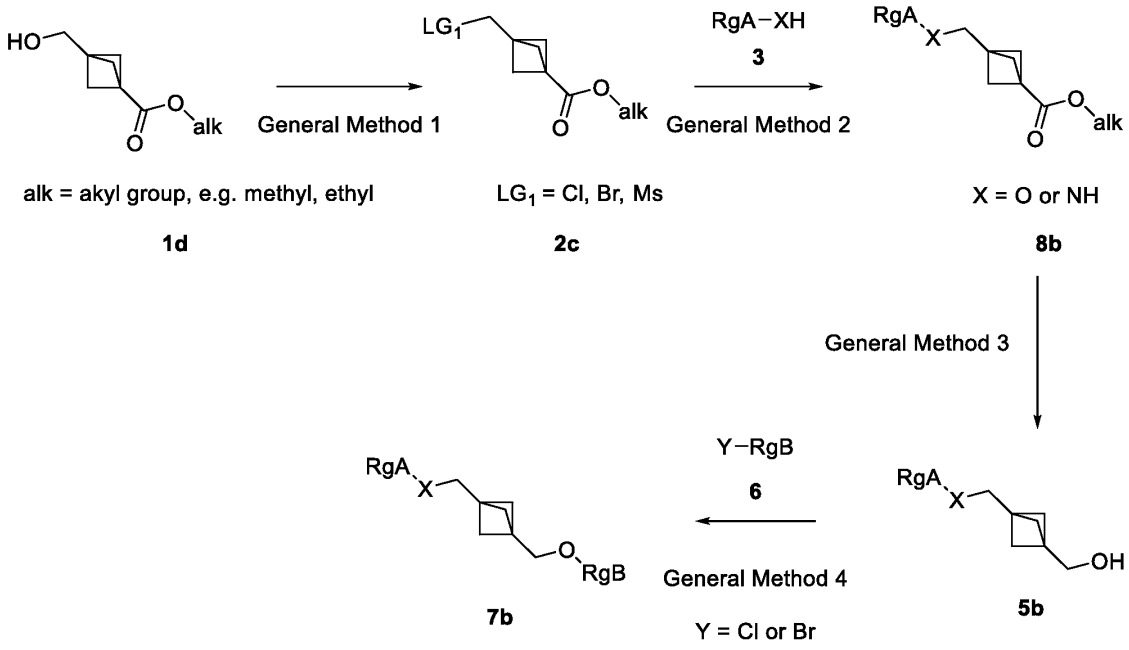
The order of steps can also be reversed, for example as shown in General Scheme 3.



General Scheme 3

An amine such as **1c** can undergo a Buchwald (General Method 4), followed by formation of a leaving group (General Method 1) and finally alkylation with compound **3** (General Method 2).

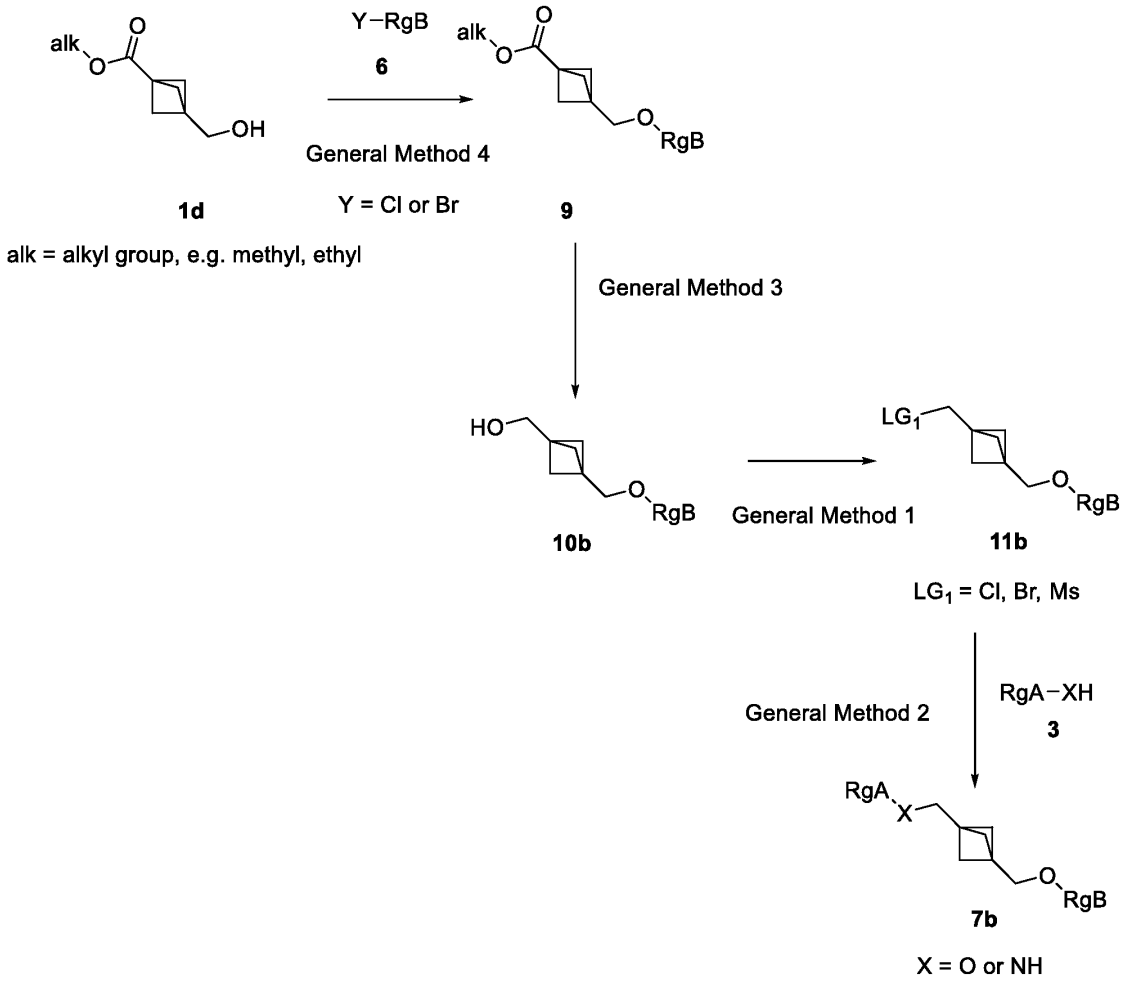
Furthermore the Buchwald coupling (General Method 4), is also possible with alcohols. This requires a suitable protecting group strategy as shown in General Schemes 4 and 5



General Scheme 4

In General Scheme 4, a protected alcohol is in the form of an ester such as **1d**. Following the usual sequence of steps, formation of a leaving group and alkylation**,** the ester **8b** is reduced using standard conditions such as $LiAlH_4$ (General Method 3) to reveal the alcohol. Finally, Buchwald coupling (General Method 4) of alcohol **5b** completes the route. This typically requires an elevated temperature, for example 90 °C or above and in some cases alternative catalysts, such as RockPhos Pd G3 are more suitable.

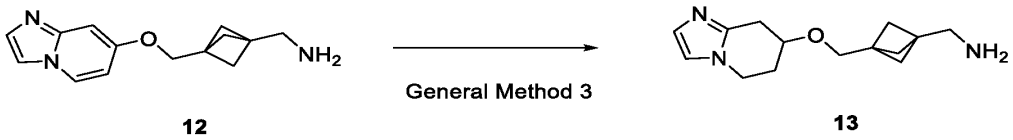
Again, the order of steps can also be reversed, for example as shown in General Scheme 5.



General Scheme 5

The alcohol such as **1d** can undergo a Buchwald (General Method 4), followed by reduction of the ester, formation of a leaving group (General Method 1) and finally alkylation with compound **3** (General Method 2).

In examples, where RgA contains a bicyclic aromatic, it can be partially saturated during the synthesis, as shown in General Scheme 6.



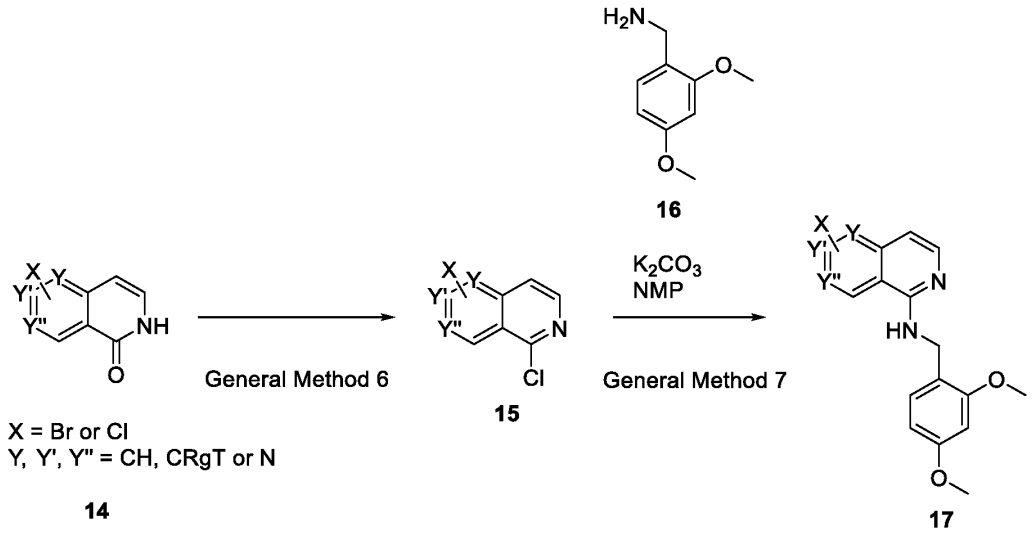
12 **13**

General Scheme 6

Typically the aromatic ring such as **12** is subjected to hydrogenation at elevated temperature (General Method 3) using H_2, 10% Pd/C to give compound **13.** This transformation can take place on the free or protected amine.

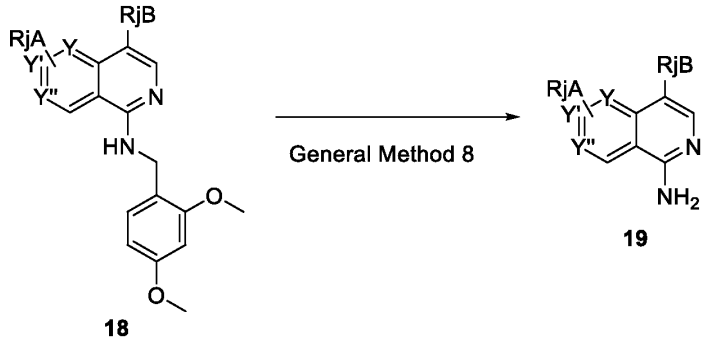
In example compounds described herein containing a primary or secondary amine, a protecting group strategy may be required. Alternative protecting groups can be used with different deprotection conditions, that is, an orthogonal protecting group strategy can be applied. General Schemes 7-12 outline possible protecting group strategies that may be used for the synthesis of the examples.

For example, for compounds defined herein containing a 6,6 ring system, as shown in General Scheme 7, a protected amine can be installed. Initially the pyridone **14** may be chlorinated, typically using phosphorous oxychloride (General method 6). The resulting chloride **15** may be reacted with 2,4-dimethoxybenzylamine using General Method 7, for example using basic conditions such as potassium carbonate or pyridine in a solvent such as NMP or MeCN, either thermally and/or under microwave conditions. RgT refers to various substituents as required by the example compounds.



General Scheme 7

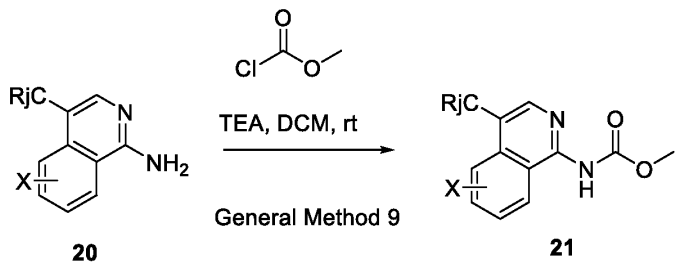
Typically, at the end of the synthetic sequence, the 2,4-dimethoxybenzyl protecting group is removed using undiluted TFA at 50 °C (General Scheme 8, General Method 8). RgT, RjA and RjB refer to various substituents as required by the examples.



Y, Y', Y'' = CH, CRgT or N

General Scheme 8

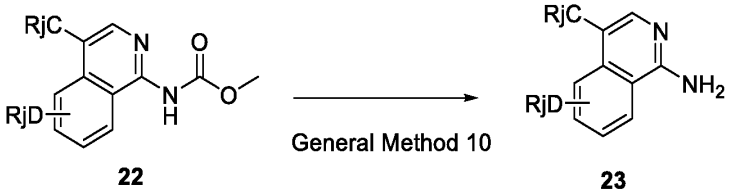
Alternatively, when starting materials are available with the amine already installed, a carbamate protecting group can be used. For example, as outlined in General Scheme 9, the amine is reacted with methyl chloroformate under basic conditions with organic bases such as TEA or DIPEA in a solvent such as DCM to afford the methyl carbamate **21** (General Method 9). RjC refers to various substituents as required by the examples.



X = Br or Cl

General Scheme 9

Typically at the end of the synthetic sequence the methyl carbamate protecting group is deprotected using basic conditions, such as KOH or LiOH in solvents such as 1,4-dioxane, MeCN, THF and optionally 10% water, at elevated temperature, typically 50 °C (General Scheme 10, General Method 10). RjC and RjD refer to various substituents as required by the examples.

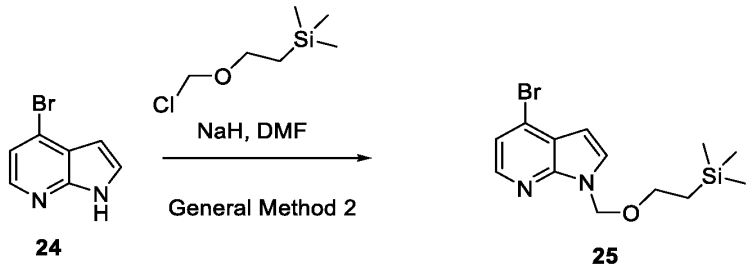


General Scheme 10

Another protecting group that may be used where example compounds described herein contain a 6,6 ring system is boc.

Where, for example, example compounds described herein contain a 5,6 ring system, SEM, boc and sulfonyl protecting groups may typically be used. Protecting groups may subsequently be deprotected using standard literature procedures, for example those described by T. W. Greene and P. G. M. Wuts in "Protective groups in organic chemistry" John Wiley and Sons, 4th Edition, 2006.

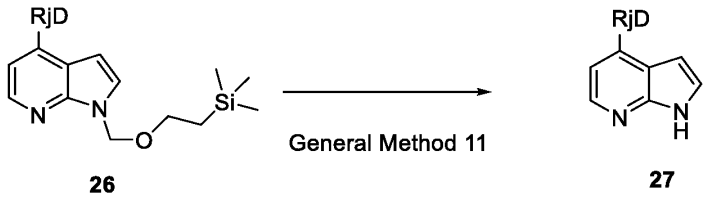
An example of the installation of a SEM protecting group is shown in General Scheme 11 whereby the indole **24** is treated with a base such as NaH in a solvent such as DMF, followed by addition of 2-(trimethylsilyl)ethoxymethyl chloride (General Method 2).



24 **25**

General Scheme 11

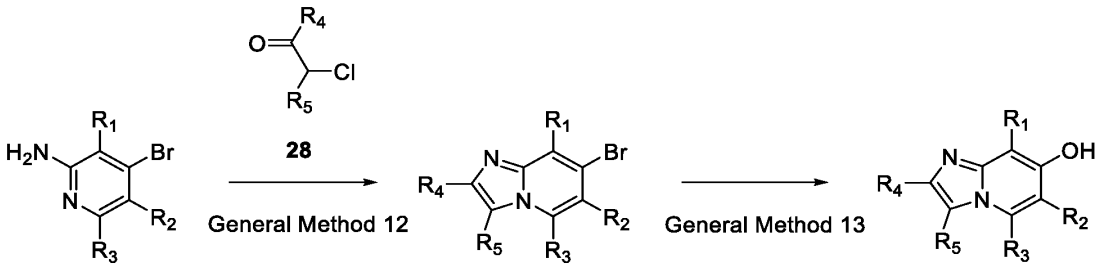
Typically at the end of the synthetic sequence the SEM protecting group is deprotected using acidic conditions such as TFA in DCM (General Scheme 12, General Method 11). RjD refers to various substituents as required by the examples.



26 **27**

General Scheme 12

In examples where RgA contains an aromatic or heteroaromatic bicycle they can be synthesised, for example, as depicted in General Scheme 13.



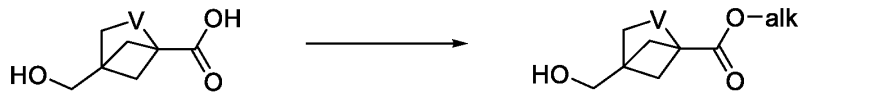
3a **3b** **3c**

R_{1-5} = alkyl, halo or H

General Scheme 13

Amino pyridines such as **3a** can be reacted with chloromethyl aldehydes and ketones **28** by refluxing in a solvent such as ethanol (General Method 12). Hydroxylation of the aryl bromide **3b** to the corresponding aryl alcohol **3c** is typically completed in a one-pot tandem process *via* Miyaura borylation (Palladium(0)-Catalyzed Cross-Coupling Reaction of Alkoxydiboron with Haloarenes: A Direct Procedure for Arylboronic Esters. T. Ishiyama, M. Murata, N. Miyaura, J. Org. Chem., 1995, 60, 7508-7510) and subsequent hydroxylation using hydrogen peroxide (General Method 13).

Other examples herein may be based on an azabicyclohexyl central core group, as shown in General Schemes 14 – 17. These General Schemes may also be applied to other central core groups such as bicyclopentyl, oxabicyclohexyl and oxabicycloheptyl. The starting materials may be readily available from commercial sources or may be known in the literature. Alternatively, some prior manipulation may be required, for example, as shown in Scheme 14, a carboxylic acid such as **1e** can be esterfied using methods generally known in the art, for example *via* formation of the acid chloride in an appropriate alcohol solvent such as methanol.



V = O, OCH_2, NH

1e

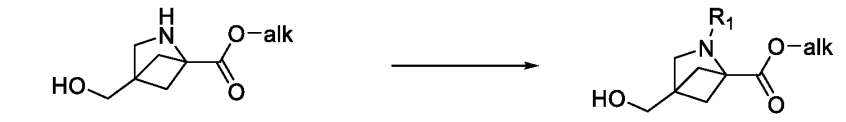
alk = akyl group, e.g. methyl, ethyl

V = O, OCH_2, NH

1d

General Scheme 14

When azabicyclohexyl rings are used they may be protected with a suitable nitrogen protecting group such as Boc or Cbz. Alternatively the nitrogen can be reacted using methods generally known in the art to provide amide, urea, alkyl and sulfonamide analogues as shown in General Scheme 15.



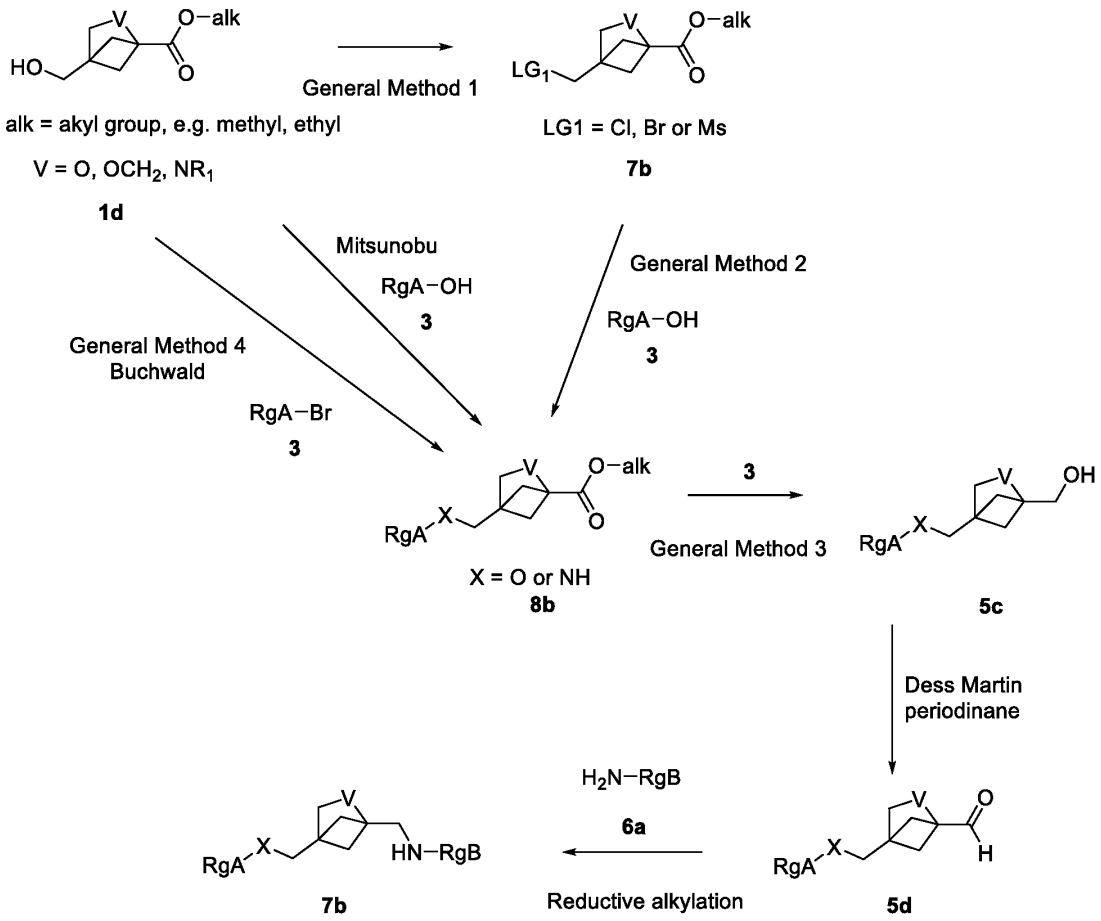
alk = akyl group, e.g. methyl, ethyl

R_1 = Cbz, boc, RG_X

1d **1f**

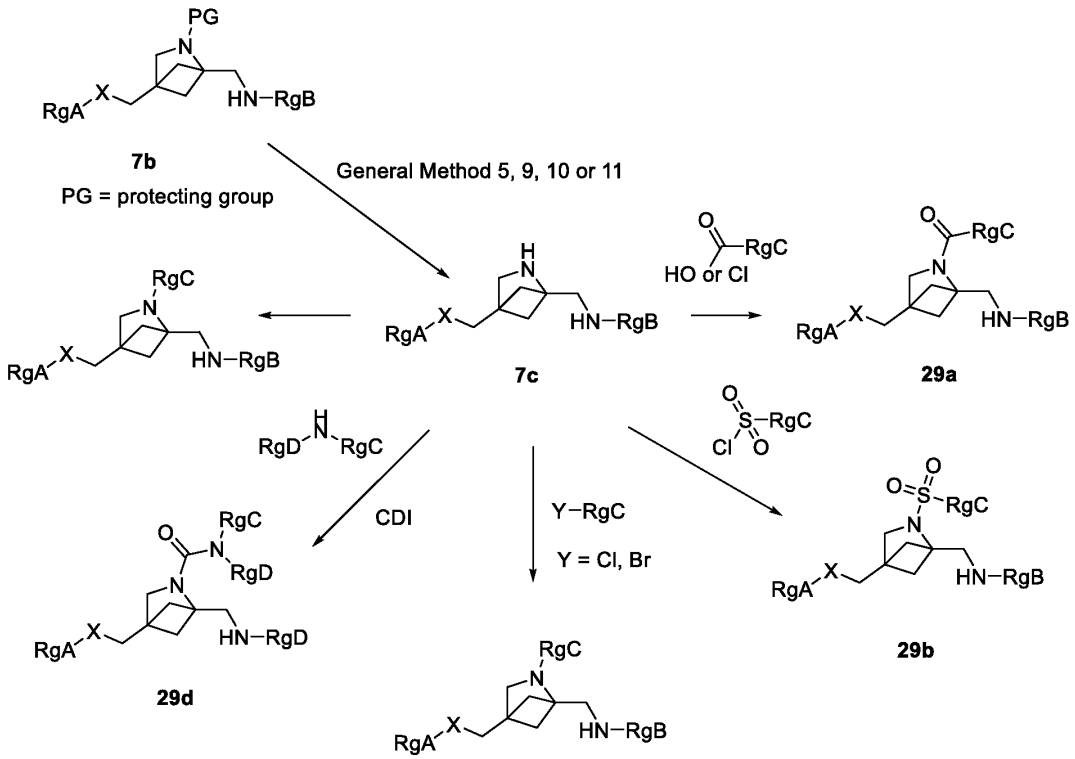
General Scheme 15

As outlined in previous schemes and as repeated in General Scheme 16, RgA can be installed by transforming the alcohol to a leaving group, such as a mesylate or halide and reacting with aryl alcohols. Alternatively the alcohol can be directly reacted with phenols under Mitsunobu conditions. The alcohol can also be coupled with aryl halides under SNAr in the presence of NaH (General Method 7a), or under Buchwald conditions (General Method 4), typically using RockPhos Pd G3 as the catalyst and elevating the temperature to 100 ℃. The ester **8b** is then reduced to alcohol **5c** under conditons well known in the art such as lithium borohydride ($LiBH_4$) or $LiAlH_4$ depending on other functionality contained in the compound. Oxidation to aldehyde **5d** is typically achieved using a reagent such as Dess Martin periodinane. Finally, reductive amination with amine **6a** completes the route. Alternatively (not shown in the Schemes) the alcohol **5c** can be transformed to an amine using methods generally known in the art, such as via conversion to a leaving group (General Method 1) then via an azide or Gabriel synthesis to provide the primary amine and finally completing the route via a Buchwald coupling (General Method 4) as shown previously in General Scheme 1.



General Scheme 16

When azabicyclohexyl rings are used, in which the nitrogen is protected by a protecting group (i.e. **7b** where V= NR_1), a late stage functionalisation is possible, as shown in General Scheme 17. The nitrogen protecting group is removed using the appropriate conditions (for example boc deprotection via General Method 5, or 2,4-dimethoxybenzyl deprotection via General Method 9, or carbamate deprotection via General Method 10, or SEM deprerotection via General Merthod 11). Manipulation of **7c** using chemistry well known in the art can provide a variety of compound classes. For example, reaction of **7c** with carboxylic acids or acid chlorides can be used to provide amides or reaction with sulphonyl chlorides can provide suphonamides. Reductive alkylation with aldehydes can give alkylated compounds. Buchwald reactions (General Method 4) or SNAr alkylation (General Method 7) with aryl halides can install aromatic groups. Reaction with CDI and alcohols can provide carbamates and with amines can provide ureas.

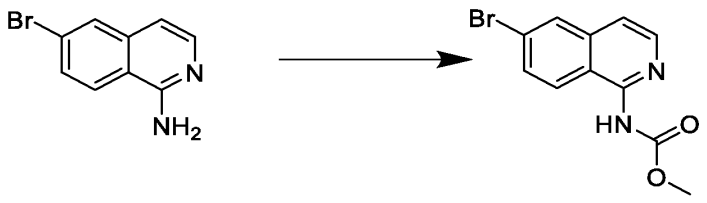


General Scheme 17

Synthesis of Intermediates

Intermediate 1

Methyl (6-bromoisoquinolin-1-yl)carbamate



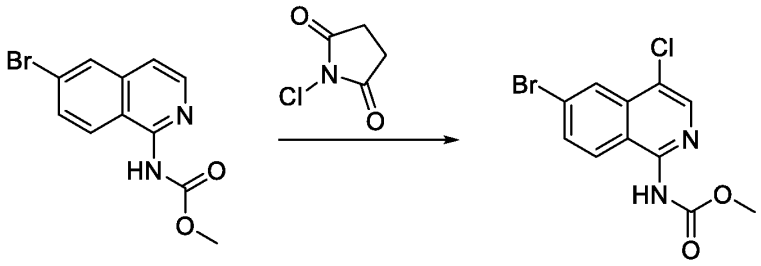
Following General Method **9**, 6-bromoisoquinolin-1-amine (1.50 g, 6.72 mmol) was protected. The crude was suspended in water (100 mL) and stirred for 30 min before being collected by filtration and dried in the vacuum oven overnight to give the product (1.12 g, 44% yield).

$[M+H]^+$ = 281.1

^{1}H NMR (500 MHz, DMSO-d6) 3.70 (3H, s), 7.58 - 7.72 (1H, m), 7.79 (1H, d, J = 9.0, 2.0 Hz), 8.04 (1H, d, J = 9.1 Hz), 8.25 - 8.30 (1H, m), 8.33 (1H, d, J = 5.8 Hz), 10.18 (1H, s)

Intermediate 2

Methyl (6-bromo-4-chloroisoquinolin-1-yl)carbamate



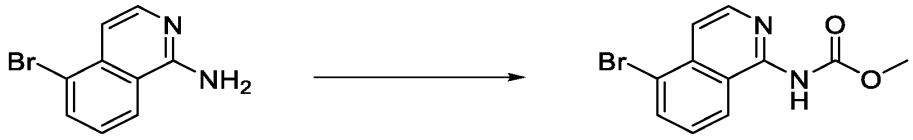
Methyl N-(6-bromo-1-isoquinolyl)carbamate (100 mg, 0.36 mmol) was dissolved in chloroform (5 mL), NCS (52 mg, 0.39 mmol) was added and the reaction stirred at reflux for 18 h. To the reaction was added sat. $NaHCO_3$ (aq.) (30 mL) and it was washed with DCM (30 mL), dried (Na_2SO_4) and concentrated. The crude product was purified by flash chromatography (Silica, 0-80% EtOAc in Pet. Ether) to give the product (74 mg, 59% yield).

$[M+H]^+$ = 316.8/318.7

^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.84 (3H, s), 7.36 (1H, s), 7.75 (1H, dd, J = 9.0, 1.9 Hz), 7.93 (1H, d, J = 9.0 Hz), 8.37 (2H, d, J = 4.9 Hz)

Intermediate 3

Methyl (5-bromoisoquinolin-1-yl)carbamate

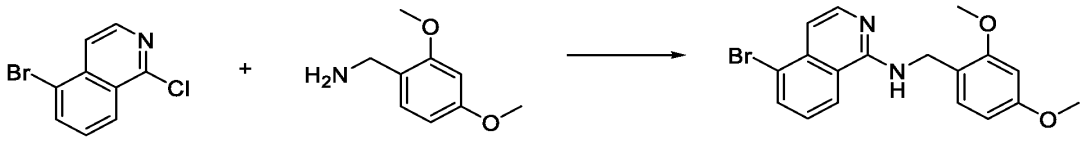


Following General Method **9**, 5-bromoisoquinolin-1-amine (1.12 g, 5.02 mmol) was protected. The product was dried under high vacuum to yield (838 mg, 56% yield)

[M+H]+ = 281.1

Intermediate 4

5-Bromo-N-(2,4-dimethoxybenzyl)isoquinolin-1-amine



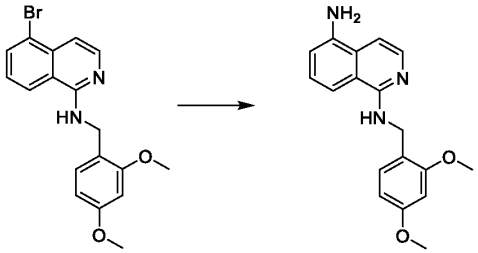
To a solution of 5-bromo-1-chloroisoquinoline (0.5 g, 2.06 mmol) in pyridine (3 mL), was added 2,4-dimethoxybenzylamine (0.69 g, 4.12 mmol). The reaction was heated at 150 °C in a CEM Microwave for 60 min. The mixture was diluted with DCM (20 mL) and water (20 mL). The aqueous layer was re-extracted with DCM (3 x 10 mL) and the combined organics were washed with brine (20 mL). The organic layer was dried (Na_2SO_4), filtered and concentrated to afford the crude product. Purification was performed by flash chromatography (Silica, 20-50% EtOAc in Pet. Ether) to afford the product (276 mg, 50% yield).

$[M+H]^+$ = 373.0/375.0

^{1}H NMR (DMSO-d_6, 400 MHz) δ 3.71 (3H, d, J = 2.6 Hz), 3.82 (3H, d, J = 2.8 Hz), 4.62 (2H, d, J = 5.4 Hz), 6.41 (1H, dd, J = 8.5, 2.5 Hz), 6.56 (1H, d, J = 2.6 Hz), 6.94 - 7.14 (2H, m), 7.42 (1H, t, J = 8.0 Hz), 7.96 (3H, ddd, J = 16.4, 7.1, 3.2 Hz), 8.38 (1H, d, J = 8.2 Hz)

Intermediate 4a

N1-(2,4-Dimethoxybenzyl)isoquinoline-1,5-diamine



A mixture of 5-bromo-N-[(2,4-dimethoxyphenyl)methyl]isoquinolin-1-amine (746 mg, 2.0 mmol), 2,2,2-trifluoroacetamide (339 mg, 3.0 mmol), CuI_2 (38 mg, 0.2 mmol), K_2CO_3 (553 mg, 4.0 mmol) and N,N'-Dimethylethylenediamine (35 mg, 0.4 mmol) were combined in a reaction vial. Anhydrous 1,4-Dioxane (7 mL) was added, and the suspension purged with N_2, before being capped and then heated to 75 °C for 24 h. The reaction was recharged with 2,2,2-trifluoroacetamide (339 mg, 3.0 mmol), CuI_2 (38 mg, 0.2 mmol), K_2CO_3 (553 mg, 4.0 mmol) and N,N'-Dimethylethylenediamine (35 mg, 0.4 mmol). The mixture was degassed with N_2 and heated at 70 °C for 18 h. Water was added (3ml) and the reaction heated at 80 °C for 6 h. The mixture was partitioned between EtOAc (30 mL) and water (10 mL). The aqueous layer was extracted with further EtOAc (2 x 30 mL) and the combined organics were washed with brine (50 mL),

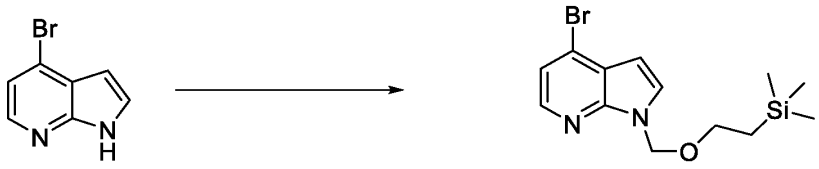
dried (Na_2SO_4), filtered and concentrated. The product was purified by flash chromatography (Silica, 0-100% EtOAc/DCM) to afford the product (492 mg, 72% yield).

$[M+H]^+$ 310.1

^1H NMR ($CDCl_3$, 400 MHz) δ 3.79 (3H, s), 3.85 (3H, s), 4.10 (2H, br s), 4.72 (2H, d, J = 5.3 Hz), 5.58 - 5.67 (1H, m), 6.44 (1H, dd, J = 8.2, 2.4 Hz), 6.49 (1H,d, J = 2.4 Hz), 6.78 - 6.86 (2H, m), 7.12 (1H, dt, J = 8.4, 1.1 Hz), 7.21 (1H, dd, J = 8.4, 7.4 Hz), 7.30 (1H, d, J = 8.2 Hz), 8.01 (1H, d, J = 6.1 Hz)

Intermediate 5

4-Bromo-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridine



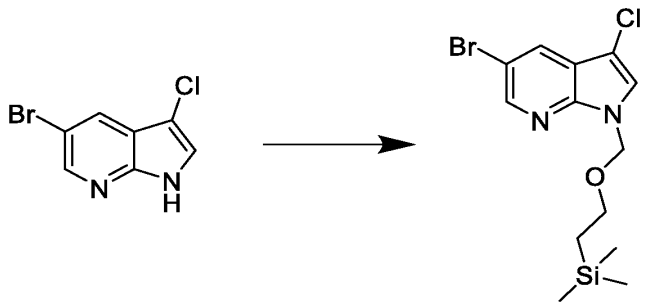
Following General Method **2a**, 4-bromo-1H-pyrrolo[2,3-b]pyridine (500 mg, 2.54 mmol) was reacted with (2-(chloromethoxy)ethyl)trimethylsilane (494 µL, 2.79 mmol) for 2 h. The reaction mixture was quenched by the careful addition of water (10 mL) followed by repeat extraction with EtOAc (3 x 20 mL). The combined organic layers were then washed with saturated $NaHCO_3$ (30 mL), water (30 mL) and brine (30 mL), before being dried ($MgSO_4$), filtered and concentrated. The crude product was purified by flash chromatography (Silica, 0-100% EtOAc in iso-hexane) to afford the product (500 mg, 57% yield) as a clear colourless oil

$[M+H]^+$ = 327.2

^1H NMR (500 MHz, DMSO-d6) δ -0.11 (s, 9H), 0.75 - 0.86 (m, 2H), 3.43 - 3.56 (m, 2H), 5.63 (s, 2H), 6.52 (d, J = 3.6 Hz, 1H), 7.43 (d, J = 5.1 Hz, 1H), 7.79 (d, J = 3.6 Hz, 1H), 8.16 (d, J = 5.1 Hz, 1H)

Intermediate 6

5-Bromo-3-chloro-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-b]pyridine



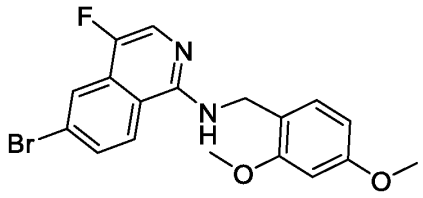
Following General Method **2a**, 5-bromo-3-chloro-1H-pyrrolo[2,3-b]pyridine (480 mg, 2.07 mmol) was reacted (2-(chloromethoxy)ethyl)trimethylsilane (0.4 mL, 2.28 mmol) for 2 h. The reaction was quenched with water (2 mL) and diluted with EtOAc (40 mL). The organic layer was washed with water (20 mL), 1M HCl (aq) (20 mL), 1:1 water/brine (20 mL) and brine (20 mL), dried ($MgSO_4$), filtered and concentrated. The crude product was purified by flash chromatography (Silica, 0-100% EtOAc in iso-hexane) to afford the product (485 mg, 60% yield).

$[M+H]^+$ = 363.0

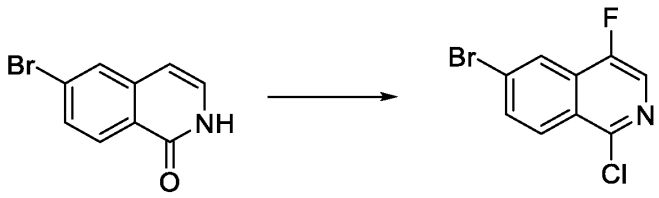
^{1}H NMR (500 MHz, DMSO-d6) δ -0.10 (9H, s), 0.81 (2H, t, J = 7.9 Hz), 3.51 (2H, t, J = 7.9 Hz), 5.60 (2H, s), 7.98 -8.01 (1H, m), 8.20 -8.24 (1H, m), 8.44 -8.47 (1H, m)

Intermediate 7

6-Bromo-N-(2,4-dimethoxybenzyl)-4-fluoroisoquinolin-1-amine



6-Bromo-1-chloro-4-fluoroisoquinoline



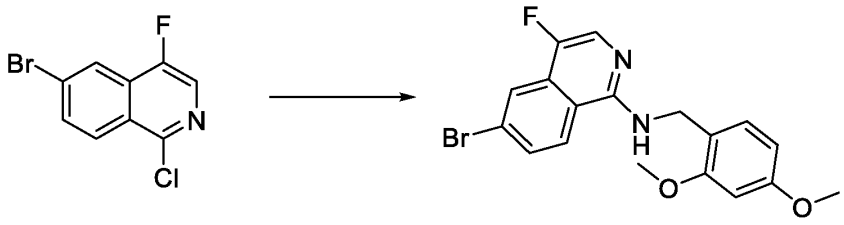
A solution of 6-bromo-2H-isoquinolin-1-one (8.0 g, 35.7 mmol) and Selectfluor (15.2 g, 42.8 mmol) in MeCN (100 mL) and MeOH (100 mL) was heated at 50 °C for 60 min. The reaction mixture was evaporated and reacted using General Method **6**, in 1,2-dichloroethane (200 mL) with benzyltriethylammonium chloride (820 mg, 3.6 mmol) and phosphorus oxychloride (50 mL). The reaction mixture was evaporated and the residue partitioned between DCM (500 mL) and water (500 mL). The organic layer was washed with water (300 mL), brine (300 mL), dried ($MgSO_4$) and evaporated. The crude was purified by flash chromatography (Silica, 5% EtOAc in Pet. Ether) to give the product (6.88 g, 74% yield).

$[M+H]^+$ = 260.0

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (d, *J* = 1.9 Hz, 1H), 8.21 – 8.16 (m, 2H), 7.84 (dd, *J* = 9.1, 1.9 Hz, 1H)

^{19}F NMR (471 MHz, $CDCl_3$) δ -139.8 (s)

6-Bromo-N-(2,4-dimethoxybenzyl)-4-fluoroisoquinolin-1-amine



Following General Method **7d**, 6-bromo-1-chloro-4-fluoroisoquinoline (6.88 g, 26.4 mmol) was reacted with 2,4-dimethoxybenzylamine (5.95 mL, 39.6 mmol) in 1-methyl-2-pyrrolidinone (100 mL) at 100 °C for 48 h. The crude product was purified by flash chromatography (Silica, 0-20% EtOAc in Pet. Ether) to give the product (3.2 g, 31% yield).

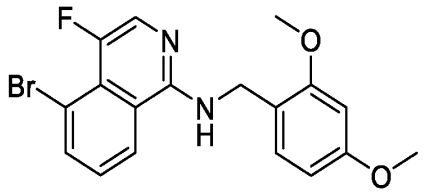
$[M-H]^-$ = 389.2

^{1}H NMR (500 MHz, DMSO) δ 8.35 (dd, *J* = 9.0, 2.2 Hz, 1H), 7.98 (d, *J* = 2.0 Hz, 1H), 7.90 – 7.70 (m, 3H), 7.07 (d, *J* = 8.3 Hz, 1H), 6.55 (d, *J* = 2.4 Hz, 1H), 6.41 (dd, *J* = 8.5, 2.4 Hz, 1H), 4.56 (d, *J* = 5.5 Hz, 2H), 3.82 (s, 3H), 3.72 (s, 3H)

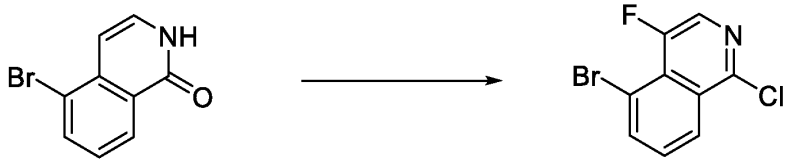
^{19}F NMR (471 MHz, DMSO) δ -157.4 (s)

Intermediate 8

5-Bromo-N-(2,4-dimethoxybenzyl)-4-fluoroisoquinolin-1-amine



5-Bromo-1-chloro-4-fluoroisoquinoline



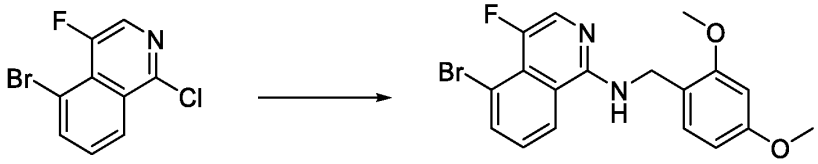
A solution of 5-bromo-2H-isoquinolin-1-one (9.0 g, 40.2 mmol) and Selectfluor (17.1 g, 48.2 mmol) in MeCN (120 mL) and MeOH (120 mL) were heated at 50 °C for 3 h. The reaction mixture was evaporated and reacted using General Method **6**, in 1,2-dichloroethane (200 mL) using benzyltriethylammonium chloride (915mg, 4.0mmol) and phosphorus oxychloride (45mL) at 90 °C for 24 h. The reaction mixture

was evaporated and the residue partitioned between DCM (500 mL) and water (500 mL). The organic layer was washed with water (300 mL) and brine (300 mL), dried ($MgSO_4$) and evaporated. The crude was purified by flash chromatography (Silica, 0-30% EtOAc in Pet. Ether) to give the product (5.70 g, 55% yield).

$[M+H]^+$ = 261.9

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.39 - 8.33 (m, 1H), 8.23 (d, J= 4.0 Hz, 1H), 8.12 –8.06 (m, 1H), 7.57 (t, J= 8.0 Hz, 1H)

5-Bromo-N-(2,4-dimethoxybenzyl)-4-fluoroisoquinolin-1-amine



Following General Method **7d**, 5-bromo-1-chloro-4-fluoroisoquinoline (5.70 g, 21.9 mmol) was reacted with 2,4-dimethoxybenzylamine (4.93 mL, 32.8 mmol) in 1-methyl-2-pyrrolidinone (80 mL) at 100 °C for 48 h. The crude product was purified by flash chromatography (Silica, 0-30% EtOAc in Pet. Ether) to give the product (1.05 g, 12% yield).

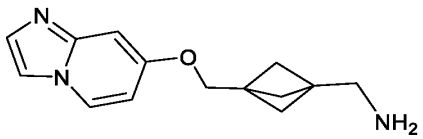
^{1}H NMR (500 MHz, DMSO) δ 8.43 (dd, J= 8.1, 2.3 Hz, 1H), 8.06 (dd, J= 7.6, 0.9 Hz, 1H), 7.89 (d, J= 5.1 Hz, 1H), 7.81 (t, J= 5.6 Hz, 1H), 7.49 (t, J= 8.0 Hz, 1H), 7.05 (d, J= 8.3 Hz, 1H), 6.56 (d, J= 2.4 Hz, 1H), 6.41 (dd, J= 8.4, 2.4 Hz, 1H), 4.57 (d, J= 5.5 Hz, 2H), 3.82 (s, 3H), 3.72 (s, 3H)

^{19}F NMR (471 MHz, DMSO) δ -149.9(s)

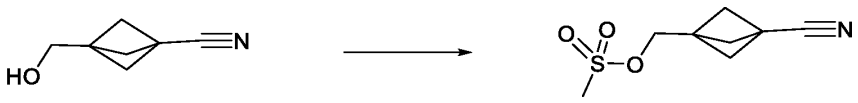
$[M-H]^-$ = 389.2

Intermediate 9

[3-(Imidazo[1,2-a]pyridin-7-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methanamine



(3-Cyano-1-bicyclo[1.1.1]pentanyl)methyl methanesulfonate

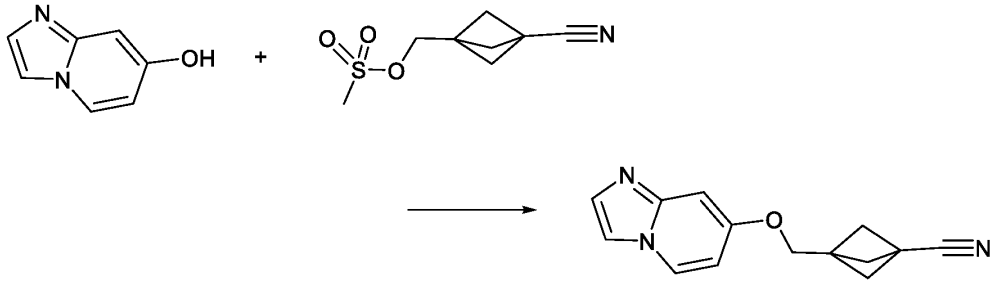


Following general method **1a,** 3-(hydroxymethyl)bicyclo[1.1.1]pentane-1-carbonitrile (320 mg, 2.6 mmol) was reacted with methane sulfonyl chloride (241 µL, 3.12 mmol) and TEA (507 µL, 3.64 mmol). The mixture

was stirred while cooling for 90 min, after which time water (30 mL) was added and the mixture extracted with DCM (2 x 50 mL), dried ($MgSO_4$), filtered and concentrated to give the product (597 mg, 100% yield).

^1H NMR (400 MHz, $CDCl_3$) δ 2.30 (s, 6H), 3.03 (s, 3H), 4.19 (s, 2H)

3-(Imidazo[1,2-a]pyridin-7-yloxymethyl)bicyclo[1.1.1]pentane-1-carbonitrile

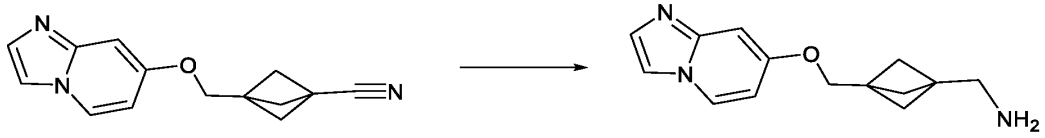


Following General Method **2a**, imidazo[1,2-a]pyridin-7-ol hydrochloride (445 mg, 2.61 mmol) was reacted with (3-cyano-1-bicyclo[1.1.1]pentanyl)methyl methanesulfonate (597 mg, 2.61 mmol) in the presence of TEA (364 µL, 2.61 mmol) for 7 days at rt. Water (30 mL) was added and the mixture extracted with EtOAc (2 x 80 mL). The combined organics were washed with brine (50 mL), dried ($MgSO_4$) and concentrated. The residue was taken up in Et_2O (5 mL) and resultant slurry was sonicated and filtered and the solid was dried *in vacuo* to afford the product (320 mg, 1.2 mmol, 46% yield).

$[M+H]^+$ = 240.1

^1H NMR ($CDCl_3$, 400 MHz) δ 2.34 (6H, s), 3.98 (2H, s), 6.50 (1H, dd, J = 7.4, 2.5 Hz), 6.75 - 6.79 (1H, m), 7.42 (1H, dd, J = 1.4, 0.7 Hz), 7.48 (1H, d, J = 1.4 Hz), 7.92 - 7.97 (1H, m)

[3-(Imidazo[1,2-a]pyridin-7-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methanamine



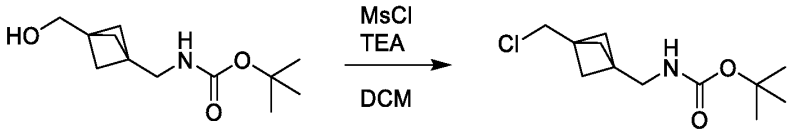
The nitrile, 3-(imidazo[1,2-a]pyridin-7-yloxymethyl)bicyclo[1.1.1]pentane-1-carbonitrile (320 mg, 1.2 mmol) was reduced following General Method **3a** using a Raney Ni CatCart. The solvent was removed *in vacuo* to afford the product (315 mg, 97% yield).

$[M+H]^+$ = 244.1

^1H NMR ($CDCl_3$, 400 MHz) δ 1.72 (6H, s), 2.76 (2H, s), 4.01 (2H, s), 6.53 (1H, dd, J = 7.4, 2.5 Hz), 6.83 (1H, d, J = 2.5 Hz), 7.37 - 7.41 (1H, m), 7.47 (1H, d, J = 1.3 Hz), 7.92 (1H, dd, J = 7.4, 0.8 Hz), NH_2 not seen

Intermediate 10

Tert-butyl N-[[3-(chloromethyl)-1-bicyclo[1.1.1]pentanyl]methyl]carbamate

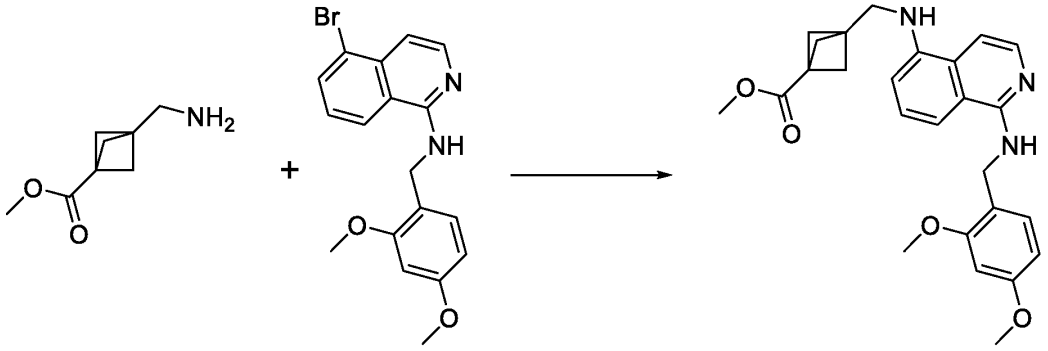


Following General Method **1b**, tert-butyl N-{[3-(hydroxymethyl)bicyclo[1.1.1]pentan-1-yl]methyl}carbamate (170 mg, 0.75 mmol) was reacted with triethylamine (188 µL, 1.35 mmol) and methane sulfonyl chloride (87 µL, 1.12 mmol) at rt for 20 h. The reaction mixture was diluted with sat. $NaHCO_3$ (aq) and the aqueous extracted with DCM (3 x 30 mL). The combined organics were washed with brine (25 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to afford the product (290 mg, 95% yield).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.44 (9H, s), 1.71 (6H, s), 3.19 (2H, d, J = 9.7 Hz), 4.20 (2H, s), 7.85 (1H, s)

Intermediate 11

Methyl 3-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]bicyclo[1.1.1]pentane-1-carboxylate

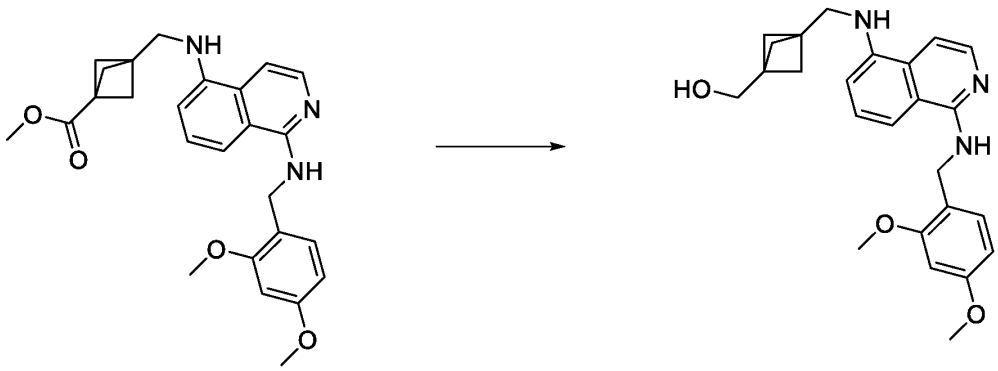


Following General Method **4**, 5-bromo-N-[(2,4-dimethoxyphenyl)methyl]isoquinolin-1-amine (389 mg, 1.04 mmol) was reacted with methyl 3-(aminomethyl)bicyclo[1.1.1]pentane-1-carboxylate hydrochloride (200 mg, 1.04 mmol) in the presence of Cs_2CO_3 (1.03 g, 3.13 mmol) in 1,4-dioxane (5 mL) at 60 °C in a sealed vial for 2 days. The reaction was concentrated onto silica and purified by flash chromatography (silica, 0 - 43% EtOAc in Pet ether) to afford the product (392 mg, 84% yield).

$[M+H]^+$ = 448.2

Intermediate 12

[3-[[[1-[(2,4-Dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-1-bicyclo[1.1.1]pentanyl]methanol



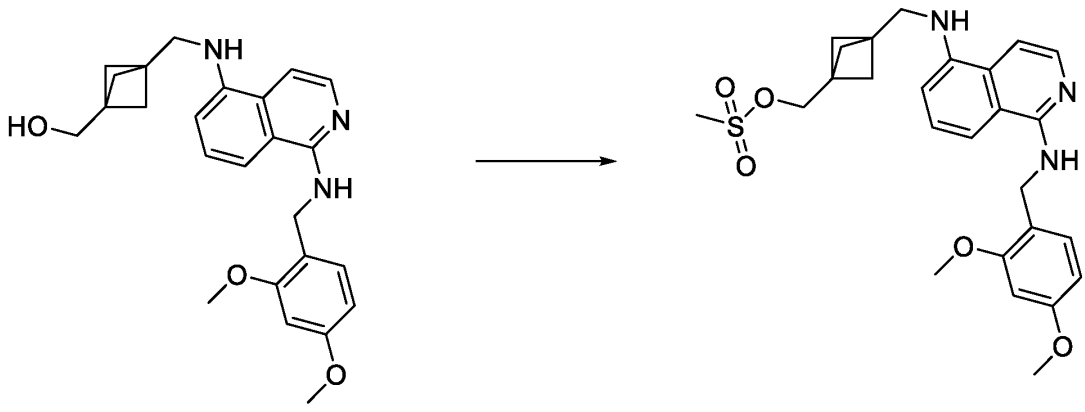
Following General Method **3b**, methyl 3-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]bicyclo[1.1.1]pentane-1-carboxylate (946 mg, 2.11 mmol) was reduced over 75 min. The product (852 mg, 96% yield) was used without purification.

$[M+H]^+$ = 420.2

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.74 (6H, s), 3.33 (2H, d, J = 5.3 Hz), 3.63 (2H, s), 3.72 - 3.76 (1H, m), 3.80 (3H, s), 3.85 (3H, s), 4.21 (1H, t, J = 5.5 Hz), 4.72 (2H, d, J = 5.3 Hz), 5.62 (1H, t, J = 5.3 Hz), 6.44 (1H, dd, J = 8.2, 2.4 Hz), 6.50 (1H, d, J = 2.4 Hz), 6.67 (1H, d, J = 7.7 Hz), 6.80 (1H, dd, J = 6.3, 0.9 Hz), 7.00 - 7.09 (1H, m), 7.22 - 7.28 (1H, m), 7.30 (1H, d, J = 8.1 Hz), 8.01 (1H, d, J = 6.1 Hz)

Intermediate 13

[3-[[[1-[(2,4-Dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-1-bicyclo[1.1.1]pentanyl]methyl methanesulfonate

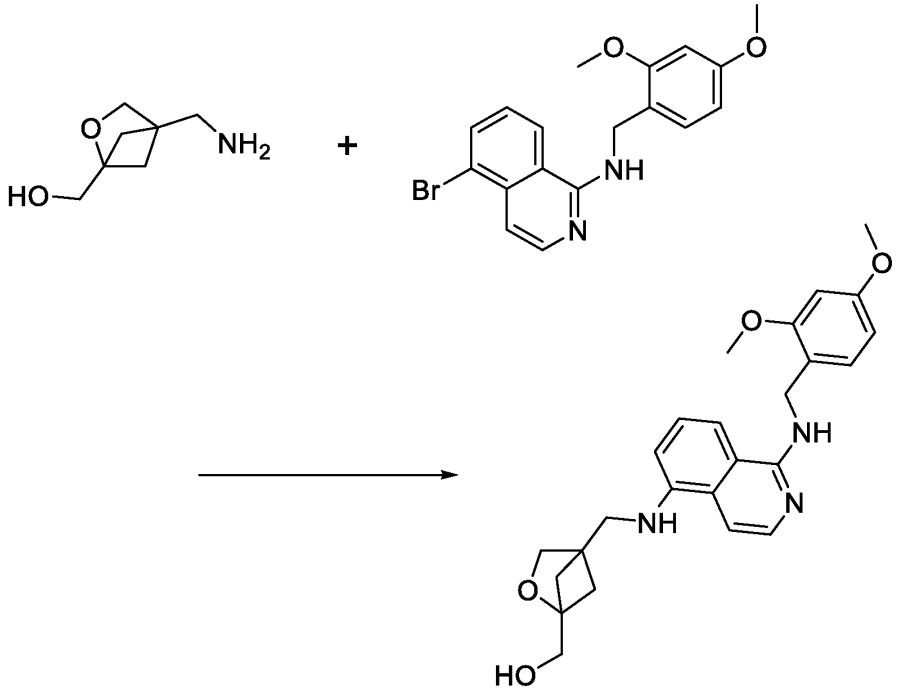


Using General Method **1a**, [3-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-1-bicyclo[1.1.1]pentanyl]methanol (450 mg, 1.07 mmol) was reacted at 0 °C for 90 min to afford the product (510 mg, 86% yield).

$[M+H]^+$ = 498.2

Intermediate 14

[4-[[[1-[(2,4-Dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-2-oxabicyclo[2.1.1]hexan-1-yl]methanol

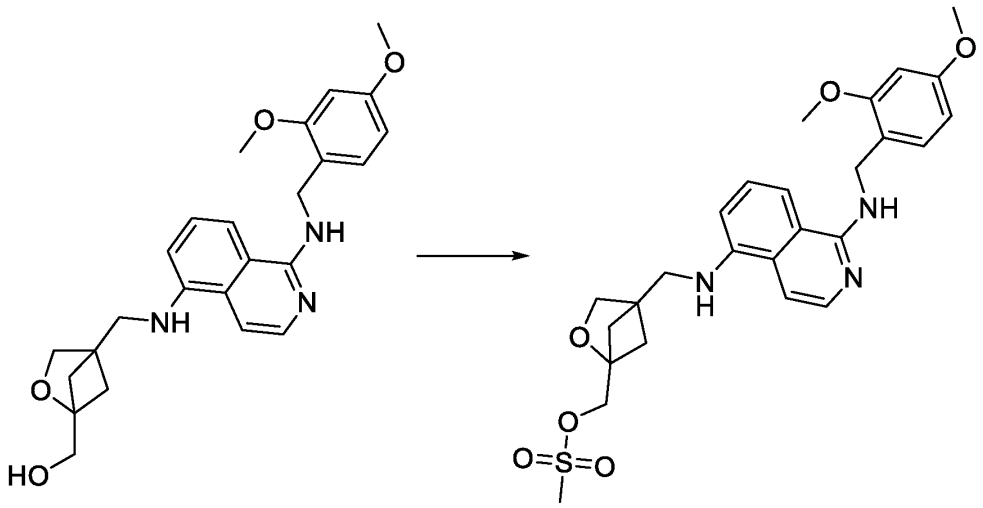


According General Method **4**, a suspension of [4-(aminomethyl)-2-oxabicyclo[2.1.1]hexan-1-yl]methanol (500 mg, 3.49 mmol), 5-bromo-N-[(2,4-dimethoxyphenyl)methyl]isoquinolin-1-amine (1434 mg, 3.84 mmol) and NaOtBu (503 mg, 5.24 mmol) in 1,4-dioxane (5 mL) was reacted in the presence of Brettphos Pd G4 (241 mg, 0.26 mmol) in a sealed vial at 40 °C for 18 h and at 60 °C for 2 h. Flash chromatography (Silica, 20-100% EtOAc in Pet. Ether) afforded the product (861 mg, 57% yield).

$[M+H]^+$ = 436.2

Intermediate 15

[4-[[[1-[(2,4-Dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-2-oxabicyclo[2.1.1]hexan-1-yl]methyl methanesulfonate

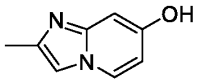


According to General Method **1a**, a solution of [4-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-2-oxabicyclo[2.1.1]hexan-1-yl]methanol (800 mg, 1.84 mmol) was reacted with methane sulfonyl chloride (252 mg, 2.2 mmol) to afford the product (914 mg, 97% yield) which was used without purification by chromatography.

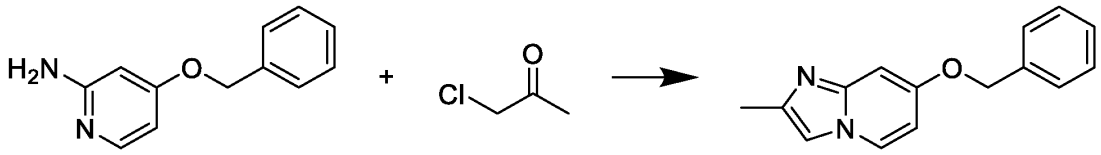
$[M+H]^+$ = 514.2

Intermediate 16

2-Methylimidazo[1,2-a]pyridin-7-ol



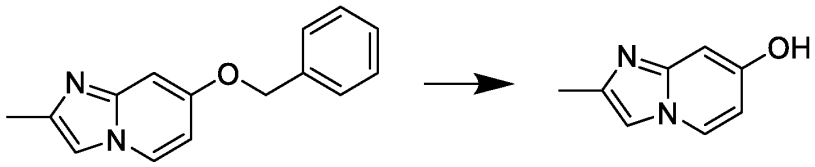
2-Methyl-7-phenylmethoxyimidazo[1,2-a]pyridine



4-(Benzyloxy)pyridin-2-amine (300 mg, 1.5 mmol) was dissolved in EtOH (5 mL). Chloroacetone (131 µL, 1.65 mmol) was added dropwise while cooling in an ice/water bath. The mixture was heated at reflux for 24 h. The solvent was removed *in vacuo* and the residue dissolved in DCM (10 mL). The organic phase was washed with sat. $NaHCO_3$ (aq) (2 x 10 mL), water (2 x 10 mL), brine (10 mL), dried ($MgSO_4$) and concentrated. Flash chromatography (SNAP KP-NH (Biotage®), 0-20% MeOH in DCM) afforded the product (131 mg, 37% yield).

^{1}H NMR (CD_3CN, 400 MHz) δ 2.32 (3H, d, J = 0.9 Hz), 5.14 (2H, s), 6.53 (1H, dd, J = 7.4, 2.5 Hz), 6.81 - 6.85 (1H, m), 7.31 (1H, q, J = 0.9 Hz), 7.36 - 7.41 (1H, m), 7.44 (2H, ddd, J = 8.0, 7.0, 1.1 Hz), 7.47 - 7.52 (2H, m), 8.06 (1H, dd, J = 7.4, 0.7 Hz) ppm.

2-Methylimidazo[1,2-a]pyridin-7-ol

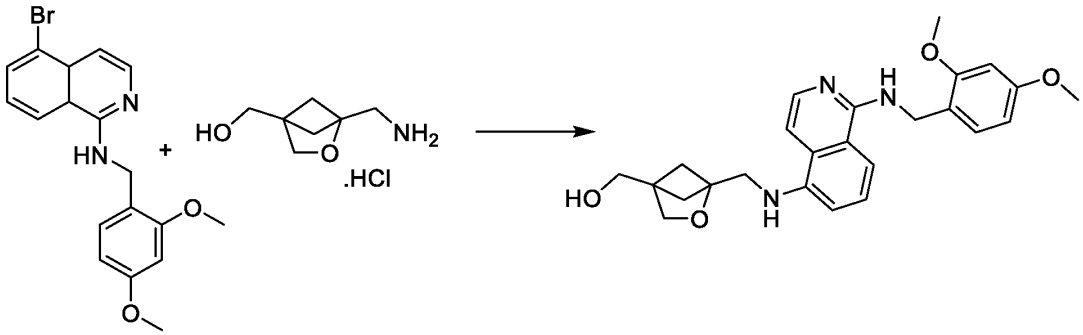


2-Methyl-7-phenylmethoxyimidazo[1,2-a]pyridine (131 mg, 0.55 mmol) was dissolved in MeOH (13 mL) and subjected to hydrogenation at 50 °C in the H-Cube at 1 mL/min using a 10% Pd/C CatCart. The solvent was removed *in vacuo.* Flash chromatography (Silica, 0-20% (10% NH_4OH in MeOH) in DCM) afforded 2-methylimidazo[1,2-a]pyridin-7-ol (39 mg, 48% yield) as a colourless oil.

$[M+H]^+$ = 149.0

Intermediate 17

[1-[[[1-[(2,4-Dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-2-oxabicyclo[2.1.1]hexan-4-yl]methanol

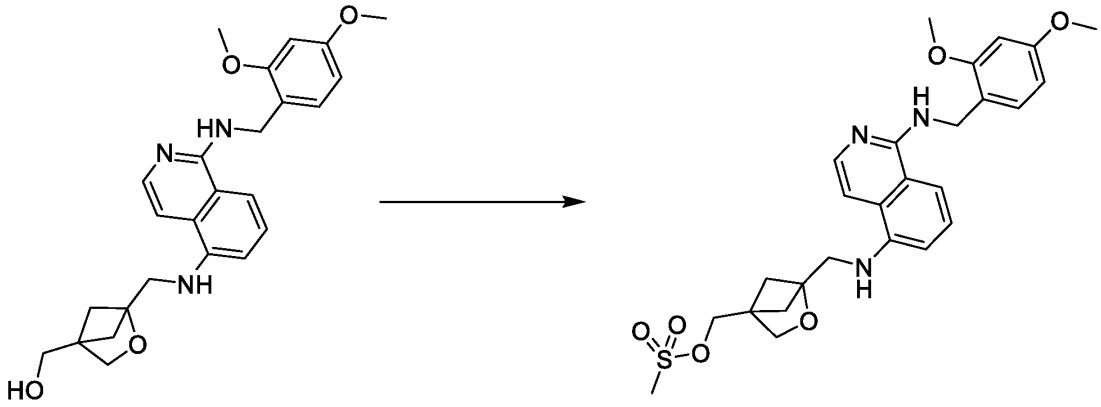


According to General Method **4**, a suspension of [1-(aminomethyl)-2-oxabicyclo[2.1.1]hexan-4-yl]methanol hydrochloride (250 mg, 1.39 mmol), 5-bromo-N-[(2,4-dimethoxyphenyl)methyl]isoquinolin-1-amine (571 mg, 1.53 mmol) and NaOtBu (334 mg, 3.48 mmol) in 1,4-dioxane (5 mL) was reacted in the presence of Brettphos Pd G4 (96 mg, 0.1 mmol) in a sealed vial at 40 °C for 18 h. Flash chromatography (Silica, 20-100% EtOAc in Pet. Ether) afforded the product (429 mg, 71% yield).

$[M+H]^+$ = 436.2

Intermediate 18

[1-[[[1-[(2,4-Dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-2-oxabicyclo[2.1.1]hexan-4-yl]methyl methanesulfonate

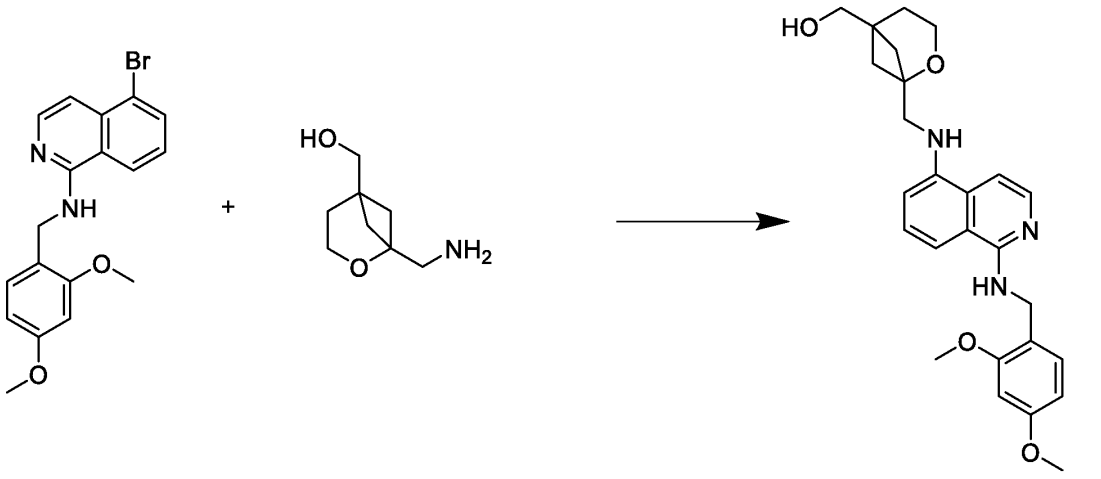


According to General Method **1a**, a solution of [1-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-2-oxabicyclo[2.1.1]hexan-4-yl]methanol (429 mg, 0.99 mmol) was reacted with methane sulfonyl chloride (135 mg, 1.18 mmol) to afford the product (440 mg, 87% yield) which was used without purification by chromatography.

LCMS: $[M+H]^+$ = 514.2

Intermediate 19

[1-[[[1-[(2,4-Dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-2-oxabicyclo[3.1.1]heptan-5-yl]methanol



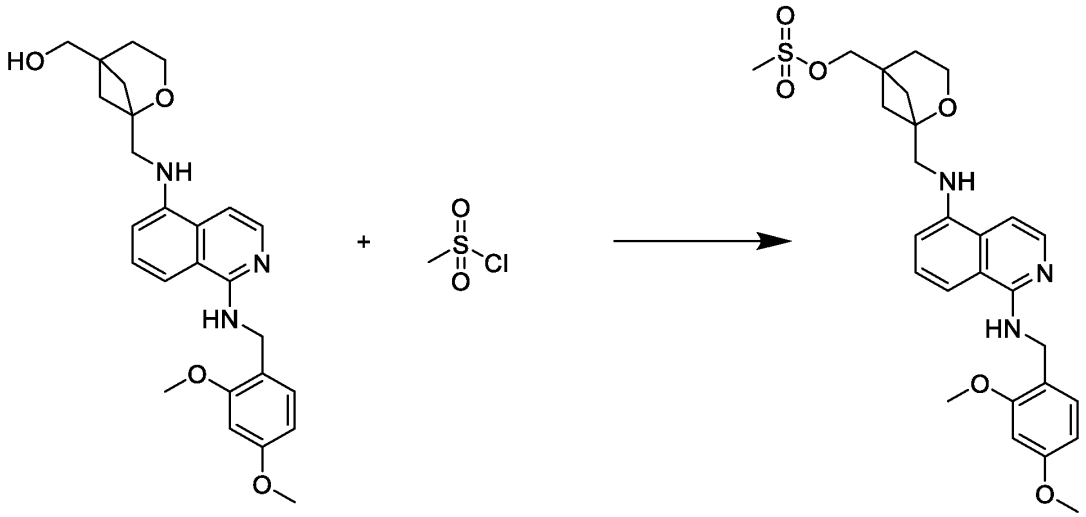
According General Method **4**, a suspension of [1-(aminomethyl)-2-oxabicyclo[3.1.1]heptan-5-yl]methanol hydrochloride (300 mg, 1.55 mmol), 5-bromo-N-[(2,4-dimethoxyphenyl)methyl]isoquinolin-1-amine (578

mg, 1.55 mmol) and NaOtBu (372 mg, 3.87 mmol) in 1,4-dioxane (6 mL) was reacted in the presence of Brettphos Pd G4 (107 mg, 0.12 mmol) in a sealed vial at 40 °C for 3 days and at 60 °C for 18 h. Flash chromatography (Silica, 0-100% EtOAc in Pet. Ether followed by 0-12% MeOH in EtOAc) afforded the product (190 mg, 27% yield).

$[M+H]^+ = 450.3$

Intermediate 20

[1-[[[1-[(2,4-Dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-2-oxabicyclo[3.1.1]heptan-5-yl]methyl methanesulfonate

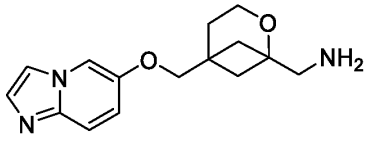


According to General Method **1a**, a solution of [1-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-2-oxabicyclo[3.1.1]heptan-5-yl]methanol (160 mg, 0.36 mmol) was reacted with methane sulfonyl chloride (36 µL, 0.46 mmol) to afford the product (190 mg, 91% yield) which was used without purification by chromatography.

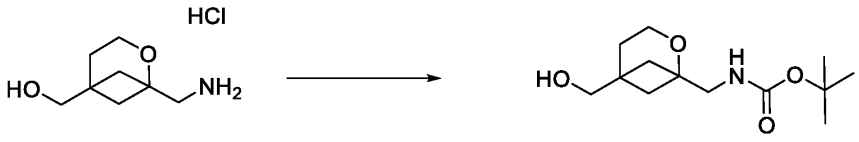
$[M+H]^+ = 528.2$

Intermediate 21

[5-(Imidazo[1,2-a]pyridin-6-yloxymethyl)-2-oxabicyclo[3.1.1]heptan-1-yl]methanamine



tert-Butyl N-[[5-(hydroxymethyl)-2-oxabicyclo[3.1.1]heptan-1-yl]methyl]carbamate

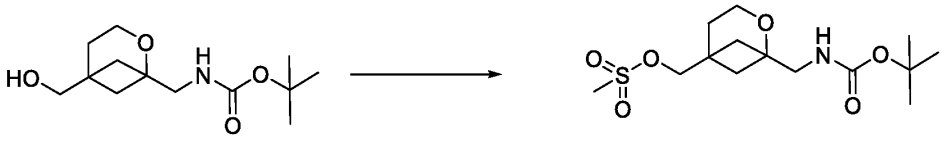


To a solution of [1-(aminomethyl)-2-oxabicyclo[3.1.1]heptan-5-yl]methanol hydrochloride (500 mg, 2.58 mmol) and TEA (1260 µL, 9.04 mmol) in THF (10 mL) at 0 °C was added Boc_2O (676 mg, 3.1 mmol) and the mixture was stirred for 10 min at 0 °C. After that time the reaction was stirred for 18 h at rt. The reaction was quenched with water (30 mL), washed with EtOAc (2 x 50 mL), dried ($MgSO_4$) and concentrated to afford the product (760 mg, 92% yield).

$[M+Na]^+ = 280.2$

^1H NMR ($CDCl_3$) δ 1.43 (9H, s), 1.74 - 1.79 (4H, m), 1.94 (2H, t, J = 6.9 Hz), 2.53 (1H, d, J = 4.4 Hz), 3.17 (2H, d, J = 5.8 Hz), 3.46 (2H, d, J = 5.5 Hz), 4.07 (2H, t, J = 6.9 Hz), 4.94 (1H, s)

[1-[[(2-Methylpropan-2-yl)oxycarbonylamino]methyl]-2-oxabicyclo[3.1.1]heptan-5-yl]methyl methanesulfonate

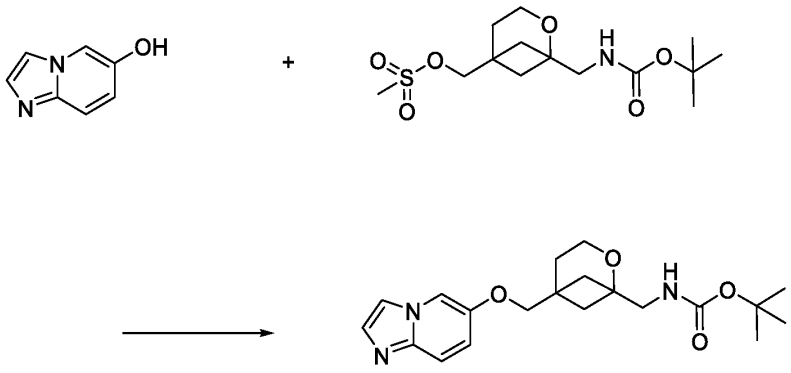


According to a modification of General Method **1a**, a solution of tert-butyl N-[[5-(hydroxymethyl)-2-oxabicyclo[3.1.1]heptan-1-yl]methyl]carbamate (760 mg, 2.36 mmol) in DCM (25 mL) was cooled in an ice bath and MsCl (219 µL, 2.84 mmol) was added dropwise followed by TEA (461 µL, 3.31 mmol) maintaining the temperature at 0 °C. The mixture was stirred at 0 °C for 90 min, after which time it was quenched with water (10 mL) and washed with DCM (2 x 10 mL), dried ($MgSO_4$) and concentrated to afford the product (950 mg, 96% yield).

$[M+Na]^+ = 358.3$

^1H NMR ($CDCl_3$) δ 1.44 (9H, s), 1.81 - 1.89 (4H, m), 2.00 (2H, t, J = 6.8 Hz), 3.02 (3H, s), 3.18 (2H, d, J = 6.0 Hz), 4.06 - 4.10 (4H, m), 4.90 (1H, s)

tert-Butyl N-[[5-(imidazo[1,2-a]pyridin-6-yloxymethyl)-2-oxabicyclo[3.1.1]heptan-1-yl]methyl]carbamate

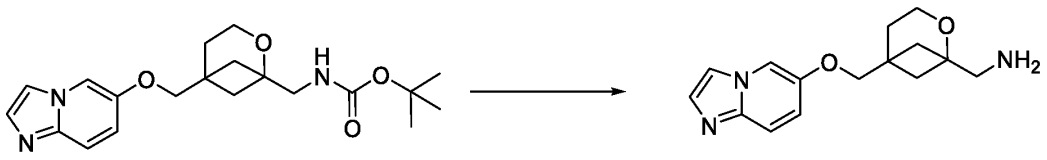


According to a modification of General Method **2b**, to a mixture of [1-[[(2-methylpropan-2-yl)oxycarbonylamino]methyl]-2-oxabicyclo[3.1.1]heptan-5-yl]methyl methanesulfonate (950 mg, 2.27 mmol) and imidazo[1,2-a]pyridin-6-ol (304 mg, 2.27 mmol) in DMF (8 mL) was added K_2CO_3 (939 mg, 6.8 mmol) at rt and the mixture was heated at 60 °C for 12 h. The reaction was cooled to rt, quenched with water (20mL) and extracted into EtOAc (2 x 40 mL). The organic layers were combined, washed with water (3 x 10 mL), brine (10 mL), dried ($MgSO_4$) and concentrated. The residue was purified by flash chromatography (Silica, 10-100% EtOAc in Pet. Ether and 0-20% MeOH in EtOAc) to afford the product (425 mg, 50% yield).

$[M+H]^+$ = 374.2

^1H NMR ($CDCl_3$) δ 1.45 (9H, s), 1.92 (4H, s), 2.07 (2H, t, J = 6.9 Hz), 3.23 (2H, d, J = 5.9 Hz), 3.74 (2H, s), 4.09 - 4.14 (2H, m), 5.03 (1H, t, J = 5.9 Hz), 6.96 (1H, dd, J = 9.7, 2.3 Hz), 7.48 - 7.51 (2H, m), 7.56 (1H, d, J = 0.8 Hz), 7.66 (1H, d, J = 1.8 Hz)

[5-(Imidazo[1,2-a]pyridin-6-yloxymethyl)-2-oxabicyclo[3.1.1]heptan-1-yl]methanamine



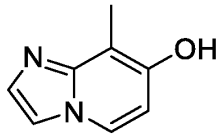
According to a modification of General Method **5b**, a solution of tert-butyl N-[[5-(imidazo[1,2-a]pyridin-6-yloxymethyl)-2-oxabicyclo[3.1.1]heptan-1-yl]methyl]carbamate (125 mg, 0.33 mmol) in DCM (3 mL) and TFA (494 µL, 6.46 mmol) was stirred at rt for 2 h, after which time it was concentrated. The mixture was taken up in MeOH and passed directly through an SCX and washed with MeOH. The product was eluted with a solution of 7M NH_3 in MeOH and concentrated to afford the product (85.0 mg, 93% yield).

$[M+H]^+$ = 274.1

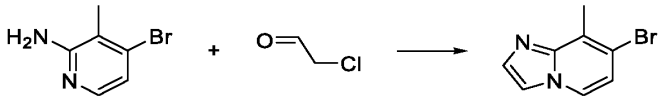
^{1}H NMR ($CDCl_3$) δ 1.51 (2H, s), 1.81 - 1.86 (2H, m), 1.91 - 1.97 (2H, m), 2.08 (2H, t, J = 6.8 Hz), 2.73 (2H, s), 3.75 (2H, s), 4.15 (2H, t, J = 6.8 Hz), 6.97 (1H, dd, J = 9.8, 2.3 Hz), 7.48 - 7.51 (2H, m), 7.56 (1H, d, J = 0.9 Hz), 7.66 (1H, d, J = 2.4 Hz)

Intermediate 22

8-Methylimidazo[1,2-a]pyridin-7-ol



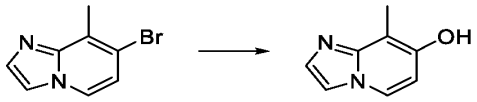
7-Bromo-8-methylimidazo[1,2-a]pyridine



According to a modification of General Method 12, to a solution of 4-bromo-3-methylpyridin-2-amine (470 mg, 2.51 mmol) in EtOH (3 mL) were added $NaHCO_3$ (422 mg, 5.03 mmol) and chloroacetaldehyde (638 µL, 5.03 mmol). The mixture was stirred for 20 h at 75 °C. The mixture was cooled to rt, filtered through Celite washing with EtOAc (50 mL) and concentrated. Flash chromatography (Silica, 50-100% EtOAc in Pet. Ether) afforded the product (431 mg, 81% yield).

$[M+H]^+$ = 211.0, 213.0

8-Methylimidazo[1,2-a]pyridin-7-ol



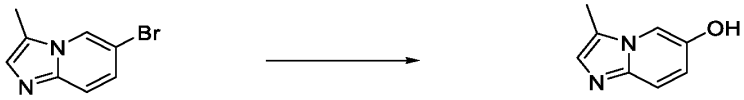
According to a modification of General Method 13, 7-bromo-8-methylimidazo[1,2-a]pyridine (431 mg, 2.04 mmol), bis(pinacolato)diboron (1167 mg, 4.59 mmol) and [1,1-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (149 mg, 0.2 mmol) were added to a screw capped vial. The vial was flushed with N_2 (g) before 1,4-dioxane (5 mL) was added. The mixture was purged with N_2 (g) for 5 min before KOAc (607 mg, 6.13 mmol) was added. The mixture was purged for a further 5 min and stirred at 100 °C for 18 h. The mixture was cooled to rt before AcOH (234 µL, 4.08 mmol) and water (1 mL) were added. The mixture was stirred for 15 min before a solution of H_2O_2 in water (30% w/w, 417 uL, 4.08 mmol) was added. The mixture was stirred for 3 h. $Na_2S_2O_3$ (5 mg) was added and the mixture

filtered through Celite and concentrated. The product was passed directly through SCX washing with MeOH. The product was eluted with a solution of 1M NH_3 in MeOH and concentrated to afford the product (92 mg, 30%) as a brown solid.

$[M+H]^+$ = 149.0

Intermediate 23

3-Methylimidazo[1,2-a]pyridin-6-ol



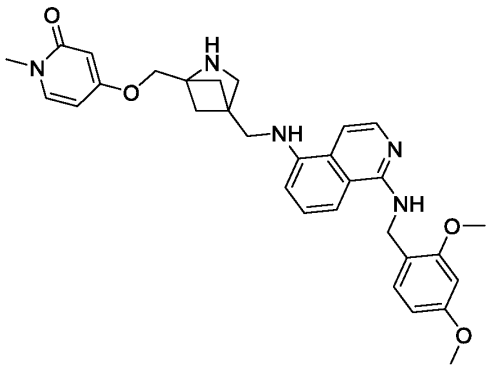
According to a modification of General Method 13, 6-bromo-3-methylimidazo[1,2-a]pyridine (525 mg, 2.49 mmol) and bis(pinacolato)diboron (1.42 g, 5.6 mmol) were suspended in 1,4-dioxane (5 mL). The mixture was purged with N_2 (g) then [1,1-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (181 mg, 0.25 mmol) was added followed by KOAc (740 mg, 7.46 mmol). The mixture was purged for a further 5 min and stirred at 100 °C for 5 h. The mixture was cooled to rt before AcOH (285 µL, 4.97 mmol) and water (1 mL) were added. The mixture was stirred for 15 min before a solution of H_2O_2 in water (30% w/w, 508 µL, 4.97 mmol) was added dropwise at 0 °C. The mixture was stirred for 90 min at rt, quenched with solid $Na_2S_2O_3$ (5 mg), filtered through Celite® and concentrated. The product was passed directly through SCX and washed with MeOH. The product was eluted with a solution of 1M NH_3 in MeOH and concentrated to afford the product (160 mg, 33% yield).

$[M+H]^+$ = 149.1

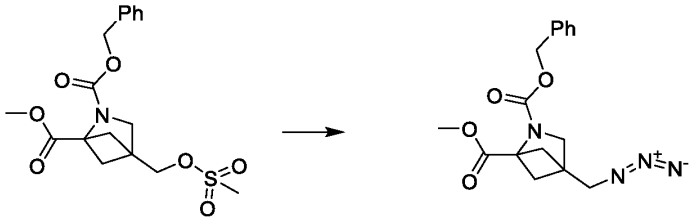
^{1}H NMR (DMSO, 400 MHz) δ 2.36 (3H, s), 6.92 (1H, dd, J = 9.6, 2.3 Hz), 7.25 (1H, s), 7.40 (1H, d, J = 9.5 Hz), 7.59 (1H, d, J = 1.9 Hz), 9.45 (1H, s)

Intermediate 24

4-((4-(((1-((2,4-Dimethoxybenzyl)amino)isoquinolin-5-yl)amino)methyl)-2-azabicyclo[2.1.1]hexan-1-yl)methoxy)-1-methylpyridin-2(1H)-one



2-O-Benzyl 1-O-methyl 4-(azidomethyl)-2-azabicyclo[2.1.1]hexane-1,2-dicarboxylate

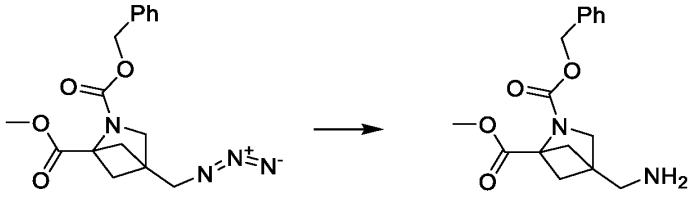


To 2-O-benzyl 1-O-methyl 4-(methylsulfonyloxymethyl)-2-azabicyclo[2.1.1]hexane-1,2-dicarboxylate (458 mg, 1.19 mmol) in DMF (5 mL) was added NaN_3 (155 mg, 2.39 mmol) at rt. The mixture was stirred at rt for 4 days. The mixture was diluted with EtOAc (50 mL) and washed with water (4 x 10 mL) and brine (10 mL), dried ($MgSO_4$) and concentrated to afford the product (330 mg, 75% yield).

$[M+H]^+ = 331.1$

^1H NMR (CD_3CN) δ 1.73 (2H, dd, J = 4.7, 1.9 Hz), 2.01 (2H, dd, J = 4.6, 1.4 Hz), 3.38 (2H, s), 3.56 (5H, s), 5.04 (2H, s), 7.28 - 7.37 (5H, m)

2-O-Benzyl 1-O-methyl 4-(azidomethyl)-2-azabicyclo[2.1.1]hexane-1,2-dicarboxylate



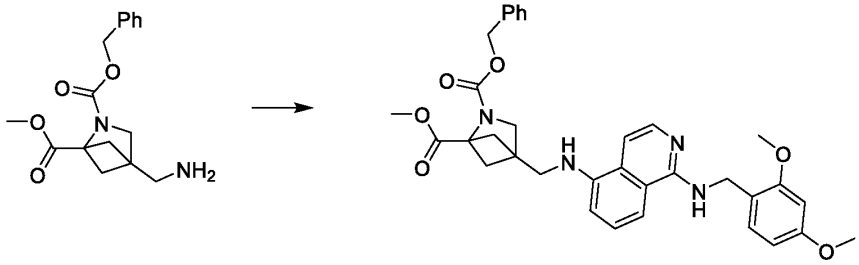
2-O-Benzyl 1-O-methyl 4-(azidomethyl)-2-azabicyclo[2.1.1]hexane-1,2-dicarboxylate (330 mg, 0.9 mmol) was dissolved in THF (6 mL). Triphenylphosphine, polymer bound (3mmol/ 1g of resin) (453 mg, 1.35 mmol) was added and the reaction stirred at rt for 2 h. Water (162 µL, 8.99 mmol) was added and the

reaction heated at reflux for 3 h. The mixture was cooled to rt and filtered, washing the resin with 10% MeOH in DCM (25 mL). The filtrate was concentrated to afford the product (240 mg, 79% yield).

$[M+H]^+$ = 305.1

^{1}H NMR ($CDCl_3$) δ 1.29 (2H, br s), 1.70 (2H, dd, J = 4.6, 1.7 Hz), 1.90 (2H, d, J = 4.6 Hz), 2.85 (2H, s), 3.34 (2H, s), 3.53 (3H, br s), 5.02 (2H, s), 7.19 - 7.28 (5H, m)

2-O-benzyl 1-O-methyl 4-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-2-azabicyclo[2.1.1]hexane-1,2-dicarboxylate

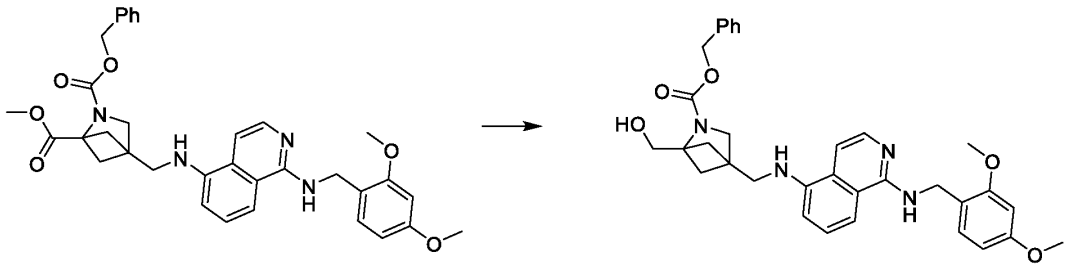


According to general method **4**, 5-bromo-N-(2,4-dimethoxybenzyl)isoquinolin-1-amine (2239 mg, 6.00 mmol) was reacted with 2-O-benzyl 1-O-methyl 4-(aminomethyl)-2-azabicyclo[2.1.1]hexane-1,2-dicarboxylate (1927 mg, 5.70 mmol), Cs_2CO_3 (5610 mg, 17.0 mmol) and Brettphos Pd G4 (801 mg, 0.852 mmol) in 1,4-dioxane (25 mL) under nitrogen. The reaction mixture was heated to 65 °C in a sealed vial for 6 h. The mixture was cooled, filtered (Celite) washing with EtOAc (200 mL), and the filtrate was concentrated. The residue was purified by flash chromatography (Silica, 0-70% EtOAc in hexanes) to afford the product (2580 mg, 76%).

$[M+H]^+$ = 597.3

^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.91 (2H, dd, J = 4.7, 1.9 Hz), 2.11 (2H, d, J = 4.8 Hz), 3.51 - 3.70 (7H, m), 3.80 (3H, s), 3.86 (3H, s), 4.26 (1H, s), 4.72 (2H, d, J = 5.3 Hz), 5.12 (2H, s), 5.63 (1H, t, J = 5.3 Hz), 6.45 (1H, dd, J = 8.3, 2.4 Hz), 6.50 (1H, d, J = 2.4 Hz), 6.66 (1H, d, J = 7.7 Hz), 6.75 (1H, d, J = 6.1 Hz), 7.08 (1H, d, J = 8.3 Hz), 7.28 - 7.39 (7H, m), 8.02 (1H, d, J = 6.1 Hz).

Benzyl 4-[[[1-[(2,4-dimethoxyphenyl)methylamino]-5-isoquinolyl]amino]methyl]-1-(hydroxymethyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate

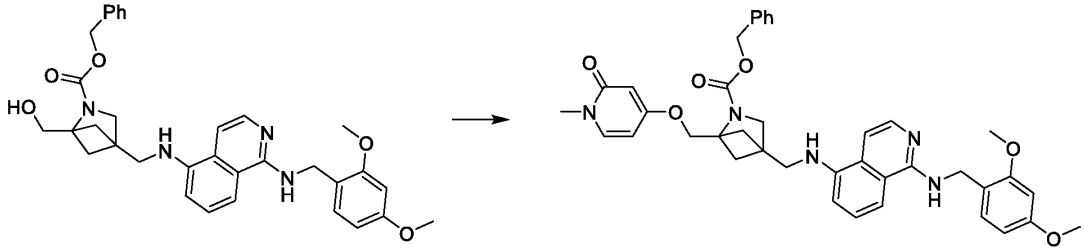


Lithium triethylborohydride (1 M in THF, 7.2 mL, 7.20 mmol) was added to a mixture of 2-O-benzyl 1-O--methyl 4-[[[1-[(2,4-dimethoxyphenyl)methylamino]-5-isoquinolyl]amino]methyl]-2-azabicyclo[2.1.1]hexane-1,2-dicarboxylate (1713 mg, 2.87 mmol) in anhydrous THF (15 mL) at 0 °C. The mixture was stirred at 0 °C for 2.5 h, and diluted with water (10 mL), brine (20 mL) and EtOAc (90 mL). The phases were separated, and the aq phase was extracted with EtOAc (2 x 50 mL). The combined organic phases were dried ($MgSO_4$) and concentrated. The residue was purified by flash chromatography (Silica, 20-68% EtOAc in hexanes) to afford the product (1096 mg, 67% yield).

$[M+H]+ = 569.8$

^1H NMR ($CDCl_3$, 400 MHz) δ 1.78 (4H, s), 3.51 (2H, s), 3.54 (2H, s), 3.80 (3H, s), 3.86 (3H, s), 3.98 (2H, d, J = 7.4 Hz), 4.24 (1H, s), 4.54 (1H, s), 4.72 (2H, d, J = 5.3 Hz), 5.14 (2H, s), 5.63 (1H, t, J = 5.4 Hz), 6.45 (1H, dd, J = 8.2, 2.4 Hz), 6.50 (1H, d, J = 2.4 Hz), 6.67 (1H, dd, J = 7.8, 0.8 Hz), 6.76 (1H, dd, J = 6.1, 0.9 Hz), 7.05 - 7.11 (1H, m), 7.37 (7H, d, J = 4.6 Hz), 8.02 (1H, d, J = 6.1 Hz).

Benzyl 4-[[[1-[(2,4-dimethoxyphenyl)methylamino]-5-isoquinolyl]amino]methyl]-1-[(1-methyl-2-oxo-4-pyridyl)oxymethyl]-2-azabicyclo[2.1.1]hexane-2-carboxylate



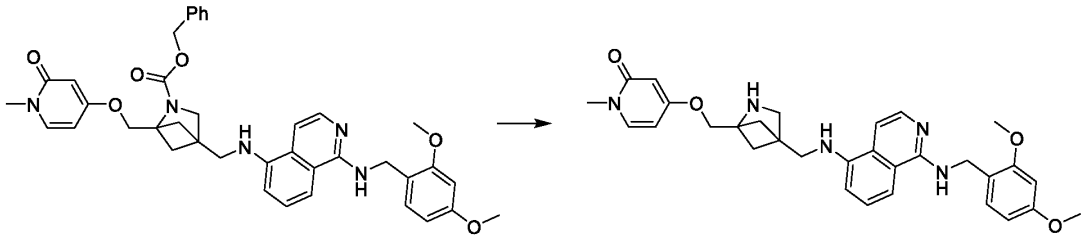
DIAD (550 µL, 2.74 mmol) was added to a mixture of benzyl 4-[[[1-[(2,4-dimethoxyphenyl)methylamino]-5-isoquinolyl]amino]methyl]-1-(hydroxymethyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate (1046 mg, 1.84 mmol), triphenylphosphine (730 mg, 2.75 mmol) and 4-hydroxy-1-methyl-pyridin-2-one (254 mg, 1.93 mmol) in anhydrous THF (15 mL) at rt. The mixture was stirred at rt for 23 h and concentrated. The residue was diluted with NaOH(aq) (1M, 20 mL) and DCM (50 mL). The phases were separated, and the aq phase was extracted with DCM (2 x 50 mL). The combined organic phases were washed with sat. $NaHCO_3$(aq) (25 mL) and brine (30 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (Silica, 0-20% MeOH in EtOAc) to afford the product (319 mg, 26% yield).

$[M+H]^+ = 676.4$

^1H NMR ($CDCl_3$, 400 MHz) δ 1.73 (2H, dd, J = 4.5, 1.9 Hz), 2.01 - 2.04 (2H, m), 3.46 (3H, s), 3.55 (2H, s), 3.57 (3H, s), 3.80 (3H, s), 3.86 (3H, s), 4.26 (1H, s), 4.47 - 4.56 (2H, m), 4.73 (2H, d, J = 5.3 Hz), 5.10 (2H, s), 5.62 (1H, d, J = 5.5 Hz), 5.82 - 5.94 (2H, m), 6.45 (1H, dd, J = 8.2, 2.4 Hz), 6.50 (1H, d, J = 2.4 Hz), 6.68 (1H, d, J =

7.7 Hz), 6.77 (1H, dd, J = 6.2, 0.9 Hz), 7.08 (2H, dd, J = 8.0, 4.4 Hz), 7.28 - 7.39 (6H, m), 8.03 (1H, d, J = 6.1 Hz).

4-[[4-[[[1-[(2,4-Dimethoxyphenyl)methylamino]-5-isoquinolyl]amino]methyl]-2-azabicyclo[2.1.1]hexan-1-yl]methoxy]-1-methyl-pyridin-2-one



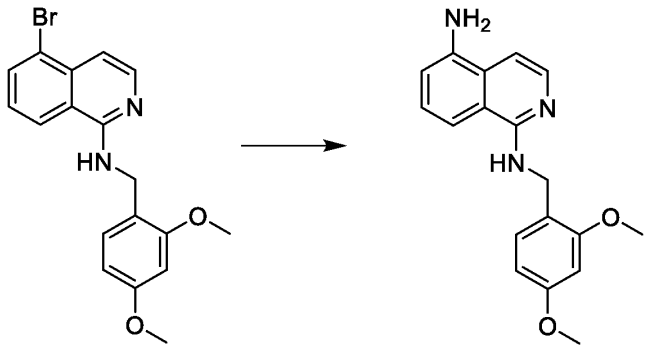
A solution of benzyl 4-[[[1-[(2,4-dimethoxyphenyl)methylamino]-5-isoquinolyl]amino]methyl]-1-[(1-methyl-2-oxo-4-pyridyl)oxymethyl]-2-azabicyclo[2.1.1]hexane-2-carboxylate (319 mg, 0.472 mmol) in MeOH (3 mL) was added to a mixture of $Pd(OH)_2/C$ (20 wt%, 82.0 mg, 0.0117 mmol) in MeOH (1.8 mL). The mixture was subjected to hydrogenation at 1 atmosphere and rt for 4 h. The mixture was filtered over Celite washing with MeOH (2 x 25 mL), and the filtrate was concentrated to afford the product (234 mg, 91%).

$[M+H]^+ = 542.4$

^1H NMR (DMSO-d6, 500 MHz) δ 1.34 (2H, dd, J = 4.0, 1.7 Hz), 1.62 (2H, dd, J = 4.2, 1.6 Hz), 2.83 (2H, s), 3.17 (1H, d, J = 2.6 Hz), 3.31 (3H+H2O, s), 3.49 (2H, d, J = 5.8 Hz), 3.71 (3H, s), 3.82 (3H, s), 4.03 (2H, s), 4.58 (2H, d, J = 5.6 Hz), 5.76 (1H, d, J = 2.8 Hz), 5.89 (1H, dd, J = 7.5, 2.8 Hz), 5.95 (1H, t, J = 6.0 Hz), 6.39 (1H, dd, J = 8.4, 2.4 Hz), 6.55 (1H, d, J = 2.4 Hz), 6.66 (1H, d, J = 7.7 Hz), 7.02 (1H, d, J = 8.4 Hz), 7.12 (1H, d, J = 6.2 Hz), 7.23 (1H, t, J = 8.0 Hz), 7.36 (1H, t, J = 5.8 Hz), 7.42 (1H, d, J = 8.4 Hz), 7.52 (1H, d, J = 7.6 Hz), 7.72 (1H, d, J = 6.0 Hz).

Intermediate 25

N1-(2,4-Dimethoxybenzyl)isoquinoline-1,5-diamine



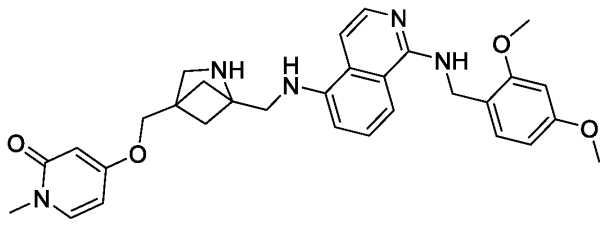
A mixture of 5-bromo-N-[(2,4-dimethoxyphenyl)methyl]isoquinolin-1-amine (746 mg, 2.0 mmol), 2,2,2-trifluoroacetamide (339 mg, 3.0 mmol), CuI_2 (38 mg, 0.2 mmol), K_2CO_3 (553 mg, 4.0 mmol) and N,N'-dimethylethylenediamine (35 mg, 0.4 mmol) were combined in a reaction vial. Anhydrous 1,4-dioxane (7 mL) was added and the suspension purged with N_2(g) before being capped and heated to 75 °C for 24 h. The reaction was recharged with 2,2,2-trifluoroacetamide (339 mg, 3.0 mmol), CuI_2 (38 mg, 0.2 mmol), K_2CO_3 (553 mg, 4.0 mmol) and N,N'-dimethylethylenediamine (35 mg, 0.4 mmol). The mixture was degassed with N_2(g) and heated at 70 °C for 18 h. Water (3 mL) was added and the reaction heated at 80 °C for 6 h. The mixture was partitioned between EtOAc (30 mL) and water (10 mL). The aqueous layer was extracted with EtOAc (2 x 30 mL) and the combined organics were washed with brine (50 mL), dried (Na_2SO_4), filtered and concentrated. Flash chromatography (Silica, 0-100% EtOAc/DCM) afforded the product (492 mg, 72% yield).

$[M+H]^+$ = 310.1

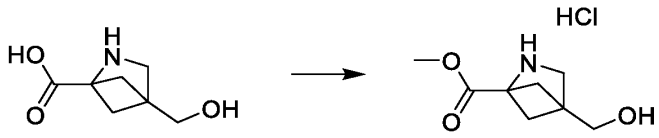
^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.79 (3H, s), 3.85 (3H, s), 4.10 (2H, br s), 4.72 (2H, d, J = 5.3 Hz), 5.58 - 5.67 (1H, m), 6.44 (1H, dd, J = 8.2, 2.4 Hz), 6.49 (1H,d, J = 2.4 Hz), 6.78 - 6.86 (2H, m), 7.12 (1H, dt, J = 8.4, 1.1 Hz), 7.21 (1H, dd, J = 8.4, 7.4 Hz), 7.30 (1H, d, J = 8.2 Hz), 8.01 (1H, d, J = 6.1 Hz)

Intermediate 26

4-((1-(((1-((2,4-Dimethoxybenzyl)amino)isoquinolin-5-yl)amino)methyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one

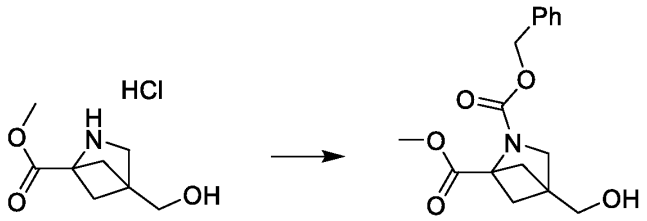


Methyl 4-(hydroxymethyl)-2-azabicyclo[2.1.1]hexane-1-carboxylate;hydrochloride



The product was prepared from 4-(hydroxymethyl)-2-azabicyclo[2.1.1]hexane-1-carboxylic acid (CAS 1522098-73-2, Tetrahedron Letters 55 (2014) 466–468) following the procedure described in ChemistrySelect 2019, 4, 4933 – 493.

2-O-Benzyl 1-O-methyl 4-(hydroxymethyl)-2-azabicyclo[2.1.1]hexane-1,2-dicarboxylate

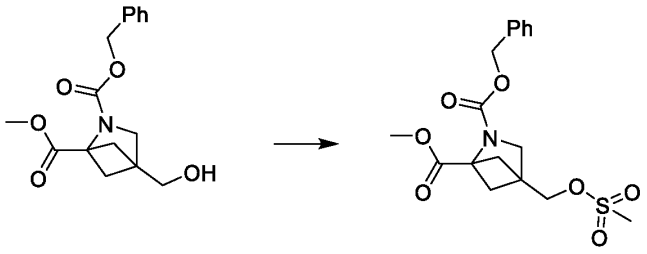


Methyl 4-(hydroxymethyl)-2-azabicyclo[2.1.1]hexane-1-carboxylate hydrochloride (600 mg, 2.89 mmol) was dissolved in DCM (15 mL) and cooled to 0 °C. TEA (805 µL, 5.78 mmol) was added followed by benzyl chloroformate (407 µL, 2.89 mmol). The reaction was stirred at rt overnight before retreating with benzyl chloroformate (200 µL, 1.42 mmol) at 0 °C and stirring at rt for an additional 1 h. DCM (30 mL) and water (10 mL) were added. The organic layer was dried ($MgSO_4$), filtered and concentrated. The crude product was purified by flash chromatography (Silica, 20-100% EtOAc in Pet. Ether) to afford the product (465 mg , 53% yield) as a colourless oil.

[M+H]+ = 306.2

^{1}H NMR (DMSO-d6, 400 MHz) δ 1.56 - 1.66 (2H, m), 1.89 - 1.97 (2H, m), 3.32 (2H, s), 3.50 - 3.65 (5H, m), 4.74 - 4.78 (1H, m), 5.04 (2H, s), 7.30 - 7.42 (5H, m)

2-O-Benzyl 1-O-methyl 4-(methylsulfonyloxymethyl)-2-azabicyclo[2.1.1]hexane-1,2-dicarboxylate

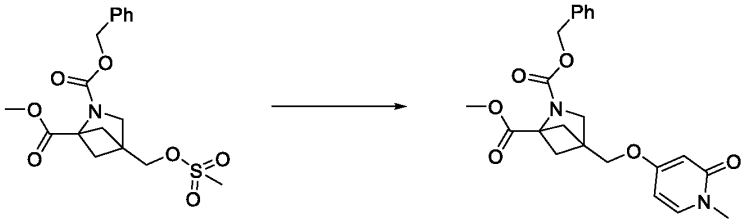


Following a modification of General Method **1a,** 2-O-benzyl 1-O-methyl 4-(hydroxymethyl)-2-azabicyclo[2.1.1]hexane-1,2-dicarboxylate (1206 mg, 3.95 mmol) was reacted with MsCl (367 µL, 4.74 mmol) and TEA (771 µL, 5.53 mmol). The mixture was stirred while cooling for 90 min, after which time water (20 mL) was added and the mixture extracted with DCM (2 x 50 mL), dried ($MgSO_4$), filtered and concentrated to give the product (1480 mg, 98% yield)

$[M+H]^+$ = 384.1.

^1H NMR ($CDCl_3$, 400 MHz) δ 1.91 (2H, dd, J = 4.8, 1.9 Hz), 2.12 (2H, dd, J = 5.0, 1.9 Hz), 3.04 (3H, s), 3.51 (2H, s), 3.67 (3H, s), 4.40 (2H, s), 5.11 (2H, s), 7.27 - 7.44 (5H, m).

2-O-Benzyl 1-O-methyl 4-[(1-methyl-2-oxopyridin-4-yl)oxymethyl]-2-azabicyclo[2.1.1]hexane-1,2-dicarboxylate

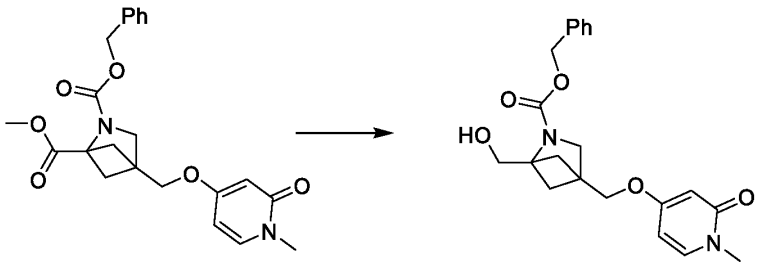


According to a modification of General Method **2b**, 2-O-benzyl 1-O-methyl 4-(methylsulfonyloxymethyl)-2-azabicyclo[2.1.1]hexane-1,2-dicarboxylate (703 mg, 1.56 mmol) was reacted with 4-hydroxy-1-methyl-2-pyridone (195 mg, 1.56 mmol) and K_2CO_3 (646 mg, 4.68 mmol) in DMF (10 mL) at 90 °C for 17 h. The reaction mixture was cooled and quenched with water (10 mL). The reaction mixture was extracted with EtOAc (3 x 20 mL). The organic layers were combined, washed with water (3 x 20 mL), dried ($MgSO_4$), and concentrated. The residue was purified by flash chromatography (Silica, 0-9% MeOH in DCM) to afford the product (620 mg, 96% yield).

$[M+H]^+$ = 413.4.

^1H NMR (DMSO-d6, 400 MHz) δ 1.74 (2H, dd, J = 4.6, 1.9 Hz), 2.10 (2H, dd, J = 4.7, 1.8 Hz), 3.32 (3H, s), 3.45 (2H, s), 3.57 (3H, s), 4.19 (2H, s), 5.06 (2H, s), 5.79 (1H, d, J = 2.8 Hz), 5.93 (1H, dd, J = 7.6, 2.8 Hz), 7.36 (5H, m), 7.56 (1H, d, J = 7.5 Hz)

Benzyl 1-(hydroxymethyl)-4-[(1-methyl-2-oxopyridin-4-yl)oxymethyl]-2-azabicyclo[2.1.1]hexane-2-carboxylate

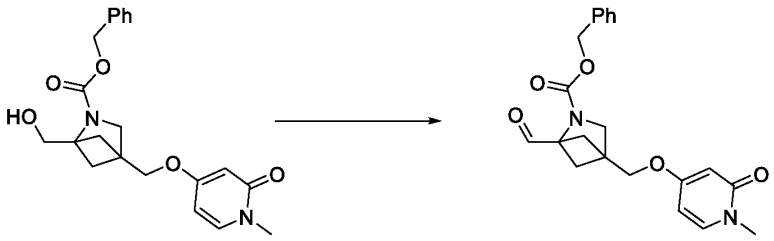


2-O-Benzyl 1-O-methyl 4-[(1-methyl-2-oxopyridin-4-yl)oxymethyl]-2-azabicyclo[2.1.1]hexane-1,2-dicarboxylate (582 mg, 1.41 mmol) was dissolved in anhydrous THF (10 mL). The solution was cooled in an ice bath and lithium borohydride ($LiBH_4$) (2M solution in THF) (776 µL, 1.55 mmol) was added. The reaction mixture was stirred at rt for 72 h after which time water (10 mL) and DCM (30 mL) were added. The organic layer was isolated and the aqueous layer re-extracted with DCM (3 x 10 mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated to afford the product (464 mg, 86% yield).

$[M+H]^+ = 385.3$

^1H NMR (DMSO-d6, 400 MHz) δ 1.46 (2H, dd, J = 4.4, 1.8 Hz), 1.83 - 1.95 (2H, m), 3.33 (3H, s), 3.41 (2H, s), 3.90 (2H, d, J = 6.1 Hz), 4.17 (2H, s), 4.70 (1H, t, J = 6.2 Hz), 5.06 (2H, s), 5.80 (1H, d, J = 2.8 Hz), 5.93 (1H, dd, J = 7.5, 2.8 Hz), 7.27 - 7.36 (1H, m), 7.37 (4H, d, J = 3.7 Hz), 7.56 (1H, d, J = 7.6 Hz)

Benzyl 1-formyl-4-[(1-methyl-2-oxopyridin-4-yl)oxymethyl]-2-azabicyclo[2.1.1]hexane-2-carboxylate

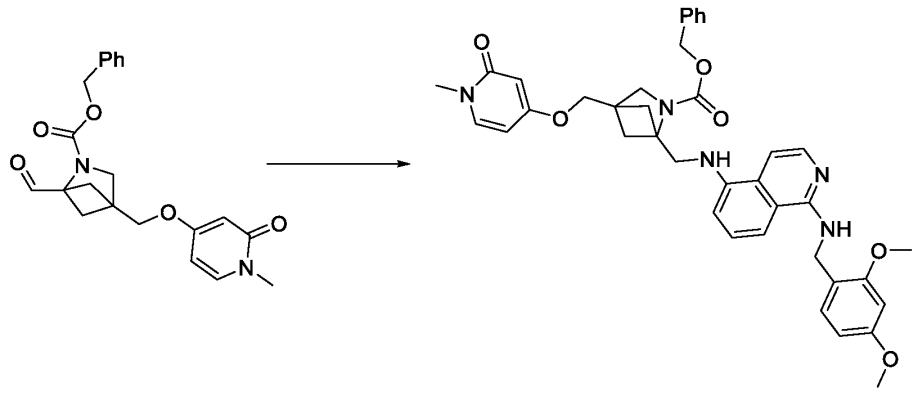


Dess-Martin periodinane (1986 mg, 4.68 mmol) was added to a solution of benzyl 1-(hydroxymethyl)-4-[(1-methyl-2-oxo-4-pyridyl)oxymethyl]-2-azabicyclo[2.1.1]hexane-2-carboxylate (1200 mg, 3.12 mmol) in DCM (30 mL) at 0 °C. The mixture was stirred at rt for 1 h. The reaction was quenched with sat. $NaHCO_3$(aq) (50 mL) and sat. $Na_2S_2O_3$(aq) (50 mL) and extracted with DCM (2 x 50 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated to afford the product (2000 mg, 99% yield).

[M+H]+ = 384.4

^1H NMR (DMSO-d6, 400 MHz) δ 1.73 (2H, dd, J = 4.4, 1.8 Hz), 2.05 (2H, d, J = 5.7 Hz), 3.32 (3H, s), 3.50 (2H, s), 4.20 (2H, s), 5.12 (2H, s), 5.80 (1H, d, J = 2.7 Hz), 5.94 (1H, dd, J = 7.5, 2.8 Hz), 7.27 - 7.44 (5H, m), 7.56 (1H, d, J = 7.6 Hz), 9.77 (1H, s)

Benzyl 1-[[[1-[(2,4-dimethoxyphenyl)methylamino]-5-isoquinolyl]amino]methyl]-4-[(1-methyl-2-oxo-4-pyridyl)oxymethyl]-2-azabicyclo[2.1.1]hexane-2-carboxylate

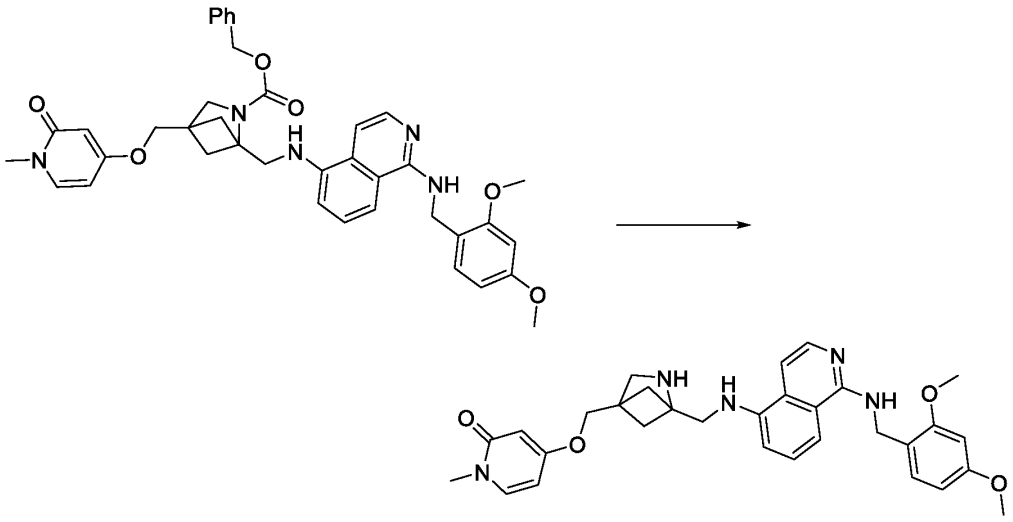


AcOH (269 µL, 4.71 mmol) was added to a mixture of benzyl 1-formyl-4-[(1-methyl-2-oxo-4-pyridyl)oxymethyl]-2-azabicyclo[2.1.1]hexane-2-carboxylate (2000 mg, 60% purity, 3.14 mmol) and N1-[(2,4-dimethoxyphenyl)methyl]isoquinoline-1,5-diamine (971 mg, 3.14 mmol) in 1,2-dichloroethane (30 mL). The mixture was stirred at rt for 30 min then STAB (1663 mg, 7.84 mmol) was added. The mixture was stirred at rt for 24 h. The reaction was quenched with sat. $NaHCO_3$(aq) (100 mL) and extracted with DCM (3 x 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated. The crude product was purified by flash chromatography (Silica, 0-30% MeOH in EtOAc) to afford the product (1600 mg, 67% yield).

[M+H]+ = 676.8

^{1}H NMR (DMSO-d6, 400 MHz) δ 1.55 (2H, d, J = 3.1 Hz), 1.91 (2H, s), 3.31 (3H, s), 3.42 (2H, d, J = 6.9 Hz), 3.71 (3H, s), 3.83 (3H, s), 3.95 (2H, d, J = 6.1 Hz), 4.13 (2H, s), 4.59 (2H, d, J = 5.6 Hz), 5.12 (2H, s), 5.76 (1H, d, J = 2.7 Hz), 5.88 (1H, dd, J = 7.5, 2.8 Hz), 6.01 (1H, s), 6.39 (1H, dd, J = 8.4, 2.4 Hz), 6.55 (1H, d, J = 2.4 Hz), 6.73 (1H, d, J = 7.7 Hz), 6.88 (1H, d, J = 6.1 Hz), 7.02 (1H, d, J = 8.4 Hz), 7.24 (1H, t, J = 8.0 Hz), 7.29 - 7.42 (6H, m), 7.46 (1H, d, J = 8.4 Hz), 7.51 (1H, d, J = 7.6 Hz), 7.71 (1H, d, J = 6.1 Hz).

4-((1-(((1-((2,4-Dimethoxybenzyl)amino)isoquinolin-5-yl)amino)methyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one



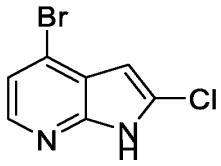
A solution of benzyl 1-[[[1-[(2,4-dimethoxyphenyl)methylamino]-5-isoquinolyl]amino]methyl]-4-[(1-methyl-2-oxo-4-pyridyl)oxymethyl]-2-azabicyclo[2.1.1]hexane-2-carboxylate (1350 mg, 2.00 mmol) in MeOH (10 mL) was added to a mixture of $Pd(OH)_2/C$ (20 wt%) (338 mg, 0.481 mmol) in MeOH (10 mL). The mixture was subjected to hydrogenation at 1 atmosphere and rt for 66 h. The mixture was filtered over Celite washing with MeOH (3 x 20 mL) and the filtrate was concentrated to afford the product (1100 mg, 95% yield).

[M+H]+ = 542.4

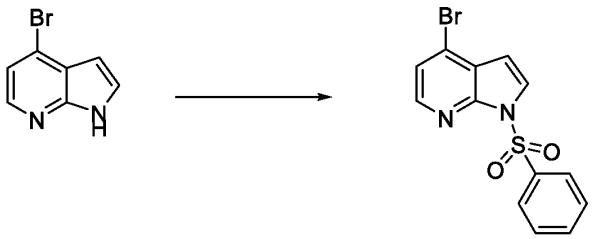
^{1}H NMR (DMSO-d6, 400 MHz) δ 1.41 (2H, s), 1.65 (2H, s), 2.87 (2H, s), 3.35 (3H, s), 3.44 (2H, d, J = 5.1 Hz), 3.71 (3H, s), 3.82 (3H, s), 4.14 (2H, s), 4.59 (2H, d, J = 5.4 Hz), 5.77 (1H, d, J = 2.7 Hz), 5.83 - 5.94 (2H, m), 6.39 (1H, dd, J = 8.4, 2.3 Hz), 6.55 (1H, d, J = 2.3 Hz), 6.68 (1H, d, J = 7.9 Hz), 7.02 (1H, d, J = 8.3 Hz), 7.08 (1H, d, J = 6.1 Hz), 7.25 (1H, s), 7.38 (1H, s), 7.45 (1H, d, J = 8.4 Hz), 7.52 (1H, d, J = 7.6 Hz), 7.73 (1H, d, J = 6.1 Hz), one exchangeable proton not observed.

Intermediate 27

1-(Benzenesulfonyl)-4-bromo-2-chloropyrrolo[2,3-b]pyridine



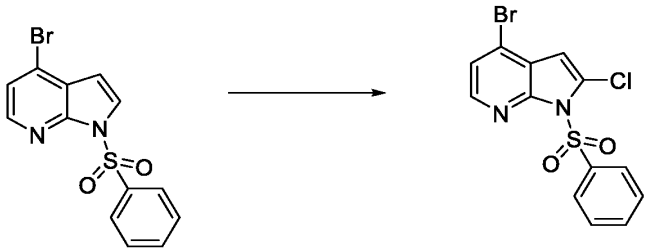
1-(Benzenesulfonyl)-4-bromopyrrolo[2,3-b]pyridine



To a solution of 4-bromo-1H-pyrrolo[2,3-b]pyridine (5.00 g, 25.4 mmol) in DCM (130 mL) was added benzenesulfonyl chloride (4.86mL, 38.1 mmol), 4-Dimethylaminopyridine (310 mg, 2.54 mmol) and TEA (10.6mL, 76.1 mmol). The reaction mixture was stirred at room temperature for 2h. Upon completion the reaction mixture was concentrated. The product was suspended in DCM (50 mL) and concentrated onto silica. The material was purified via flash chromatography (Silica, 0-50% EtOAc in Pet. Ether) to afford the product (8.39 g, 98% yield).

$[M+H]^+ = 338.9$

1-(Benzenesulfonyl)-4-bromo-2-chloropyrrolo[2,3-b]pyridine

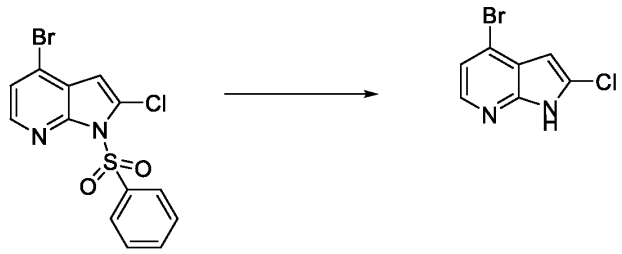


1-(Benzenesulfonyl)-4-bromopyrrolo[2,3-b]pyridine (1.00g, 2.97 mmol) in anhydrous THF (16 mL) was cooled to -41 °C and lithium diisopropylamide (2M in THF) (356 mL, 7.12 mmol) was added slowly. The resulting precipitate was stirred for 30 minutes at -41 °C before benzenesulfonyl chloride (757 µL, 5.93 mmol) was added. The reaction mixture was stirred for 2.5 h at -41 °C.

The reaction mixture was quenched with 10 mL water and diluted with 20 mL EtOAc. The layers were separated and the aq layer was back extracted with EtOAc (2 x 20 mL). The organic layers were combined, washed with brine (10 mL), dried ($MgSO_4$), filtered and concentrated. The product was purified via flash chromatography (Silica, 0-60% EtOAc in Pet. Ether) to afford the product (895 mg, 49% yield).

$[M+H]^+ = 372.9$

1-(Benzenesulfonyl)-4-bromo-2-chloropyrrolo[2,3-b]pyridine



1-(Benzenesulfonyl)-4-bromo-2-chloropyrrolo[2,3-b]pyridine (895 mg, 1.44 mmol) was taken up in 1,4-Dioxane (7 mL) and NaOtBu (324 mg, 2.89 mmol) was added. The reaction mixture was stirred at 80 °C for 2 h, diluted with EtOAc (10 mL) and washed with brine (10 mL). Layers were separated and the organic layer was dried ($MgSO_4$), filtered and concentrated. The crude material was purified via flash chromatography (Silica, 0-25% EtOAc in Pet. Ether) to afford the product (295 mg, 88% yield).

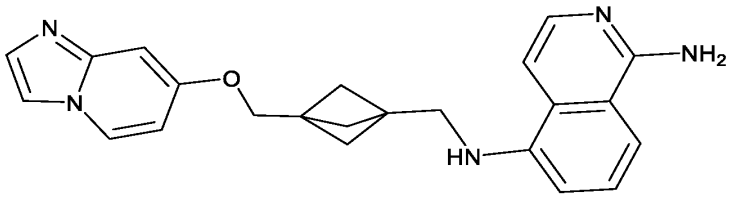
$[M+H]^+ = 232.9$

^1H NMR ($CDCl_3$, 400 MHz) δ 6.47 (1H, s), 7.32 (1H, d, J = 5.3 Hz), 8.11 (1H, d, J = 5.3 Hz*)* NH proton not observed

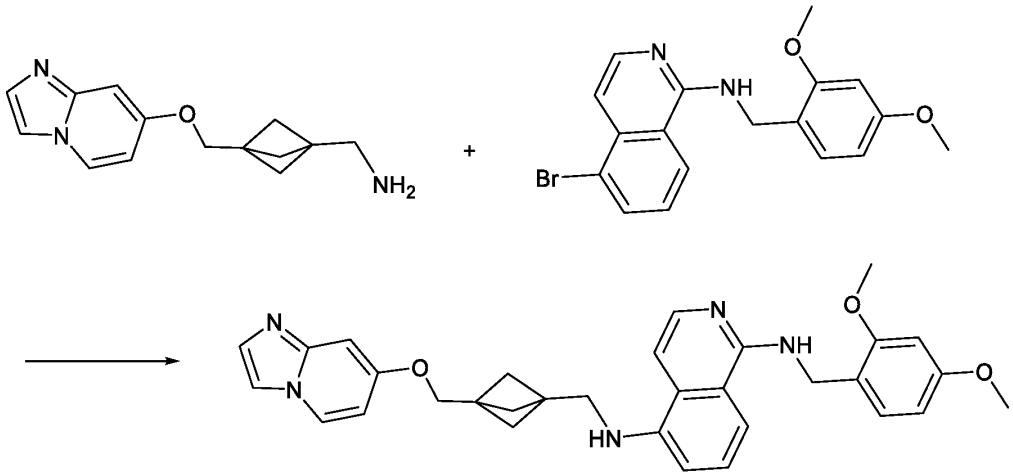
Specific Examples of the Present Invention

Example number 1001

N5-((3-((Imidazo[1,2-a]pyridin-7-yloxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine



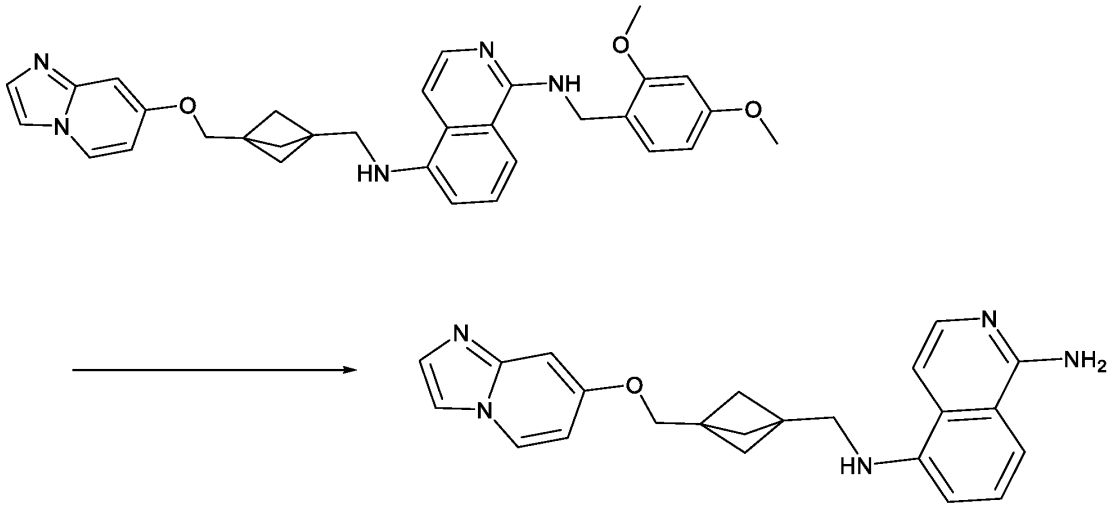
N1-[(2,4-dimethoxyphenyl)methyl]-N5-[[3-(imidazo[1,2-a]pyridin-7-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methyl]isoquinoline-1,5-diamine



Using General Method **4**, [3-(imidazo[1,2-a]pyridin-7-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methanamine (100 mg, 0.37 mmol) was reacted with 5-bromo-N-(2,4-dimethoxybenzyl)isoquinolin-1-amine (138 mg, 0.37 mmol) and NaOtBu (71 mg, 0.74 mmol) in 1,4-dioxane (5 mL) in the presence of BrettPhos Pd G3 (34 mg, 0.04 mmol) in a sealed vial at 90 °C for 6 h. The reaction was cooled and concentrated onto silica. The residue was purified by flash chromatography (Silica, 0-15% MeOH in DCM) to afford the product (70 mg, 35% yield).

$[M+H]^+$ = 536.3

N5-((3-((Imidazo[1,2-a]pyridin-7-yloxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine (Example 1001)



N1-[(2,4-dimethoxyphenyl)methyl]-N5-[[3-(imidazo[1,2-a]pyridin-7-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methyl]isoquinoline-1,5-diamine (70 mg, 0.13 mmol) was deprotected according

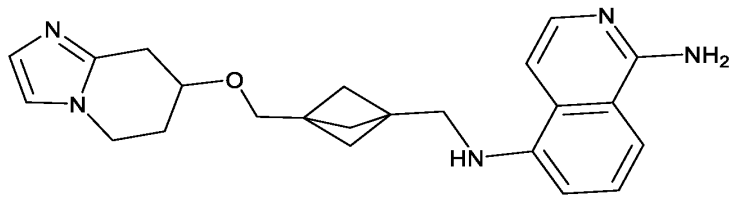
to General Method **8** in TFA (1 mL, 8.63 mmol) at rt for 60 min. The solvent was removed *in vacuo*. The crude residue was suspended in MeOH (2 mL) and loaded on to a 2 g SCX-2 column, which was flushed with MeOH (10 mL), followed by 1N NH_3 in MeOH (10 mL) to elute the crude product. The crude product was purified by automated prep HPLC (mass directed 2-60% MeCN in water with a basic mobile phase of 0.1% NH_3 in water over 20 min) and lyophilized to afford the product (20 mg, 39% yield).

$[M+H]^+$ = 386.2

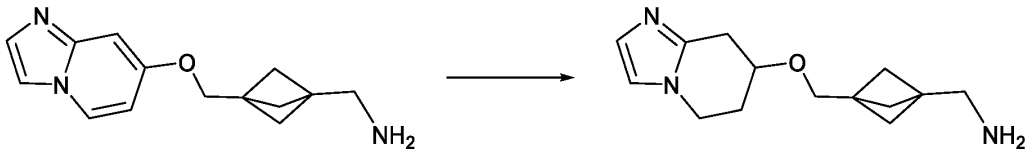
^{1}H NMR (DMSO, 400 MHz) δ 1.75 (6H, s), 4.04 (2H, s), 5.87 (1H, t, J = 5.9 Hz), 6.47 (2H, s), 6.56 (1H, dd, J = 7.4, 2.5 Hz), 6.65 (1H, d, J = 7.7 Hz), 6.87 (1H, d, J = 2.5 Hz), 7.11 - 7.16 (1H, m), 7.19 (1H, t, J = 8.0 Hz), 7.31 (1H, d, J = 8.3 Hz), 7.36 (1H, d, J = 1.3 Hz), 7.63 - 7.75 (2H, m), 8.35 (1H, dd, J = 7.4, 0.6 Hz)

Example numbers 1002, 1002.1 and 1002.2

N5-((3-(((5,6,7,8-Tetrahydroimidazo[1,2-a]pyridin-7-yl)oxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine



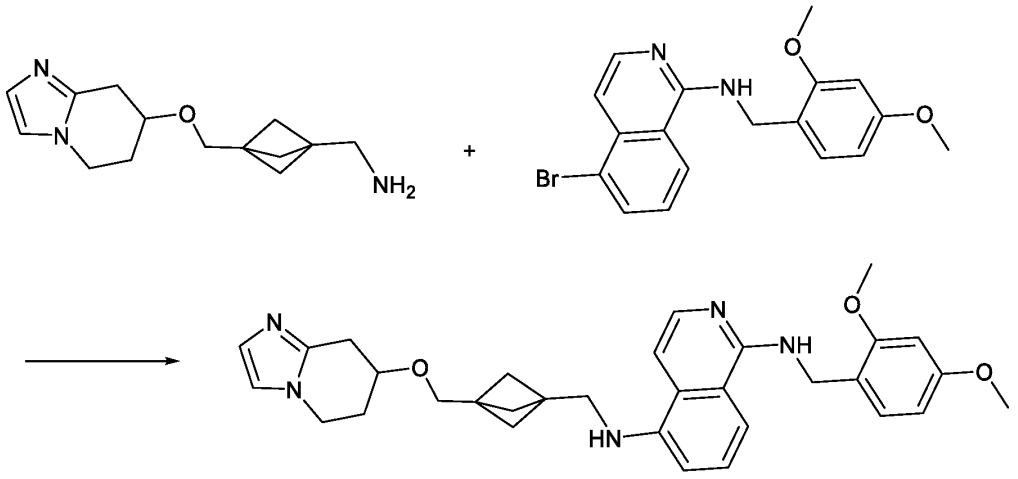
[3-(5,6,7,8-Tetrahydroimidazo[1,2-a]pyridin-7-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methanamine



[3-(imidazo[1,2-a]pyridin-7-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methanamine (100 mg, 0.41 mmol) was dissolved in EtOH (10 mL) and subjected to hydrogenation in the H-Cube® at 70 °C, 50 bar, 1 mL/min using a 10% Pd/C CatCart. After 6 passes, the solvent was removed *in vacuo* to afford the product (70 mg, 55% yield).

$[M+H]^+$ = 248.1

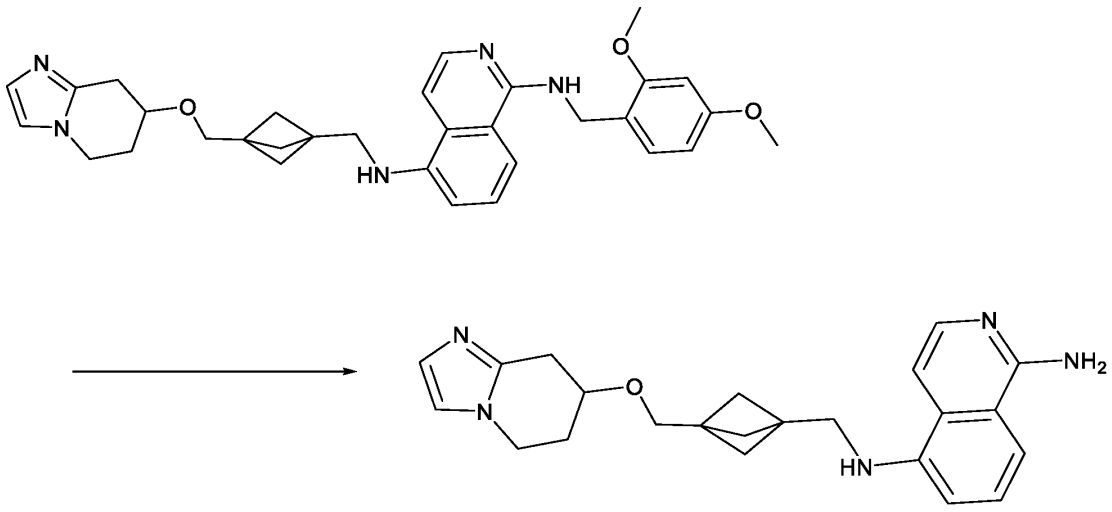
N1-[(2,4-Dimethoxyphenyl)methyl]-N5-[[3-(5,6,7,8-tetrahydroimidazo[1,2-a]pyridin-7-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methyl]isoquinoline-1,5-diamine



Using General Method **4**, [3-(5,6,7,8-tetrahydroimidazo[1,2-a]pyridin-7-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methanamine (64 mg, 0.21 mmol) was reacted with 5-bromo-N-(2,4-dimethoxybenzyl)isoquinolin-1-amine (77 mg, 0.21 mmol) in 1,4-dioxane (5 mL) in the presence of NaOtBu (40 mg, 0.41 mmol) and BrettPhos Pd G4 (19 mg, 0.02 mmol), in a sealed vial at 90 °C for 18 h. After that time, the reaction was cooled, filtered through Celite® and the filter washed with EtOAc (50 mL) and MeOH (5 mL) and the combined filtrates concentrated *in vacuo*. The residue was purified by flash chromatography (Silica, 0-100% DCM in Pet. Ether followed by 0-20% MeOH in DCM) to afford the product (22 mg, 20% yield).

$[M+H]^+$ = 540.3

N5-((3-(((5,6,7,8-Tetrahydroimidazo[1,2-a]pyridin-7-yl)oxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine (Example 1002)



N1-[(2,4-Dimethoxyphenyl)methyl]-N5-[[3-(5,6,7,8-tetrahydroimidazo[1,2-a]pyridin-7-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methyl]isoquinoline-1,5-diamine (22 mg, 0.04 mmol) was deprotected according to General Method **8**, in TFA (0.46 mL, 6.11 mmol) at rt and for 3 h. The solvent was removed *in vacuo*. The crude residue was suspended in MeOH (2 mL) and loaded onto a 2 g SCX-2 column, which was flushed with MeOH (10 mL), followed by 7N NH_3 in MeOH (2 x 10 mL) to elute the crude compound. The crude product was purified by automated prep HPLC (mass directed 2-60% MeCN in water with a basic mobile phase of 0.1% NH_3 in water over 20 min) and lyophilized to afford the product.

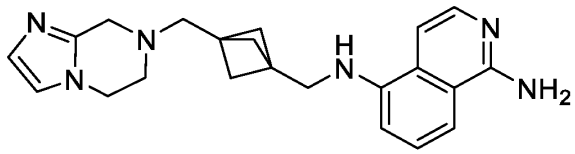
LCMS: $[M+H]^+$ = 390.2

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.74 (6H, s), 2.04 - 2.17 (2H, m), 2.96 (1H, dd, J = 16.8, 5.8 Hz), 3.08 (1H, dd, J = 16.7, 4.7 Hz), 3.32 (2H, d, J = 3.6 Hz), 3.47 - 3.59 (2H, m), 3.84 - 3.96 (2H, m), 4.05 - 4.14 (1H, m), 4.22 (1H, s), 5.18 (2H, s), 6.71 (1H, dd, J = 7.7, 0.8 Hz), 6.79 (1H, d, J = 1.3 Hz), 6.93 (1H, dd, J = 6.2, 1.0 Hz), 6.99 (1H, d, J = 1.3 Hz), 7.11 (1H, dt, J = 8.5, 1.0 Hz), 7.34 (1H, t, J = 8.0 Hz), 7.91 (1H, d, J = 6.2 Hz)

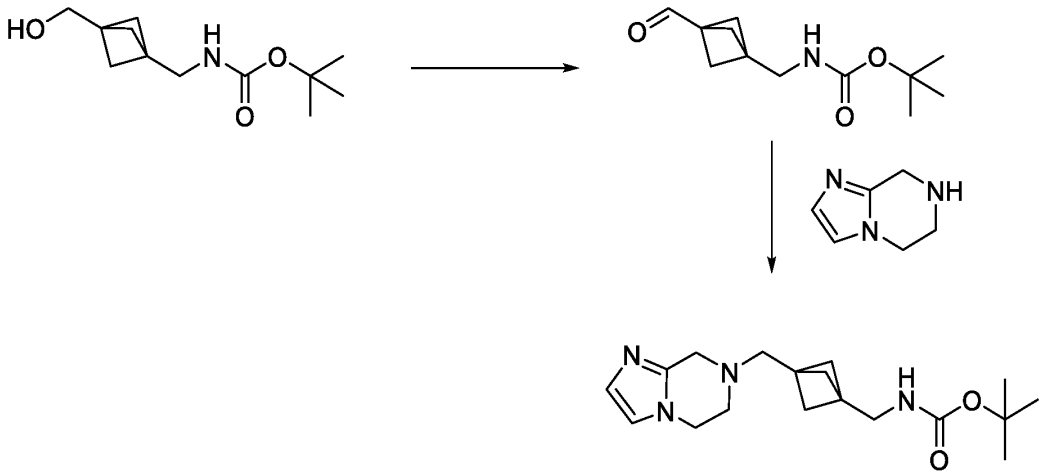
(S*)-N5-((3-(((5,6,7,8-Tetrahydroimidazo[1,2-a]pyridin-7-yl)oxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine (Example 1002.1) and (R*)-N5-((3-(((5,6,7,8-tetrahydroimidazo[1,2-a]pyridin-7-yl)oxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine (Example 1002.2) were prepared by chiral separation of the racemate N5-((3-(((5,6,7,8-tetrahydroimidazo[1,2-a]pyridin-7-yl)oxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine (Example 1002).

Example number 1004

5-N-[[3-(6,8-Dihydro-5H-imidazo[1,2-a]pyrazin-7-ylmethyl)-1-bicyclo[1.1.1]pentanyl]methyl]isoquinoline-1,5-diamine



Tert-butyl N-[[3-(6,8-dihydro-5H-imidazo[1,2-a]pyrazin-7-ylmethyl)-1-bicyclo[1.1.1]pentanyl]methyl]carbamate



Tert-Butyl N-{[3-(hydroxymethyl)bicyclo[1.1.1]pentan-1-yl]methyl}carbamate (100 mg, 0.44 mmol) was taken up in DCM (5 mL) while cooling in an ice/water bath. Dess-Martin periodinane (261 mg, 0.62 mmol) was added and the mixture stirred at rt for 3 h. Sat. $Na_2S_2O_3$ (aq) (5 mL) and sat. $NaHCO_3$ (aq) (5 mL), were added and the mixture stirred for 15 min and extracted with DCM (3 x 20 mL). The combined organics were washed with brine (10 mL), dried ($MgSO_4$) and concentrated. The residue was suspended in THF (10 mL). 5,6,7,8-Tetrahydroimidazo[1,2-a]pyrazine (60 mg, 0.48 mmol) was added and the reaction was stirred for 15 min. STAB (278 mg, 1.32 mmol) was added and the mixture was stirred at rt for 18 h. Water (10 mL) was added and the mixture extracted with DCM (3 x 10 mL). The combined organics were washed with brine (10 mL), dried ($MgSO_4$) and concentrated. The residue was passed directly through an SCX and washed with MeOH. The product was eluted with a solution of 1M NH_3 in MeOH and concentrated to afford the product (75 mg, 51% yield).

$[M+H]^+$ = 333.2

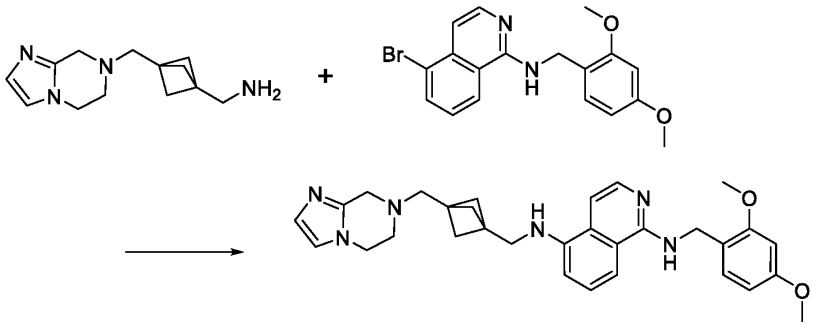
[3-(6,8-Dihydro-5H-imidazo[1,2-a]pyrazin-7-ylmethyl)-1-bicyclo[1.1.1]pentanyl]methanamine



tert-ButylN-[[3-(6,8-dihydro-5H-imidazo[1,2-a]pyrazin-7-ylmethyl)-1-bicyclo[1.1.1]pentanyl]methyl]carbamate (75 mg, 0.23 mmol) was treated with 4M HCl in dioxane according to General Method **5a**, and purified according to Method (ii), to afford the product (66 mg, 99% yield).

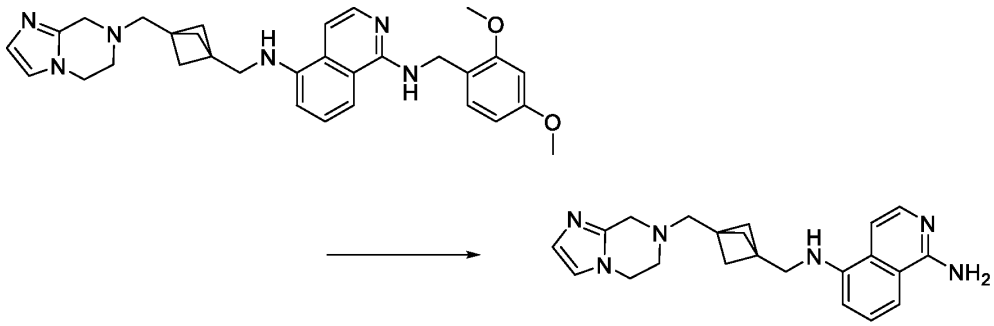
$[M+H]^+$ = 233.1

5-N-[[3-(6,8-Dihydro-5H-imidazo[1,2-a]pyrazin-7-ylmethyl)-1-bicyclo[1.1.1]pentanyl]methyl]-1-N-[(2,4-dimethoxyphenyl)methyl]isoquinoline-1,5-diamine



5-Bromo-N-[(2,4-dimethoxyphenyl)methyl]isoquinolin-1-amine (106 mg, 0.28 mmol) and [3-(6,8-dihydro-5H-imidazo[1,2-a]pyrazin-7-ylmethyl)-1-bicyclo[1.1.1]pentanyl]methanamine (66 mg, 0.28 mmol) were reacted according to General Method **4** in the presence of Brettphos Pd G4 and Cs_2CO_3. Flash chromatography (Silica, 0 - 20% (10% NH_4OH in MeOH) in EtOAc) afforded the product (53 mg, 36%. $[M+H]^+$ = 525.3

5-N-[[3-(6,8-Dihydro-5H-imidazo[1,2-a]pyrazin-7-ylmethyl)-1-bicyclo[1.1.1]pentanyl]methyl]isoquinoline-1,5-diamine (Example 1004)



5-N-[[3-(6,8-Dihydro-5H-imidazo[1,2-a]pyrazin-7-ylmethyl)-1-bicyclo[1.1.1]pentanyl]methyl]-1-N-[(2,4-dimethoxyphenyl)methyl]isoquinoline-1,5-diamine (53 mg , 0.1 mmol) was deprotected using General Method **8**. The mixture was cooled to rt and the solvent was removed *in vacuo*, azeotroping with toluene. The residue was dissolved in MeOH (3 mL) and passed directly through SCX-2 and flushed with MeOH (3 x 5 mL). The product was eluted with a solution of 1M NH_3 in MeOH (3 x 5 mL) and the solvent was removed *in vacuo*. The product was purified by flash chromatography (Silica, 0-20% (10% NH_4OH in MeOH)

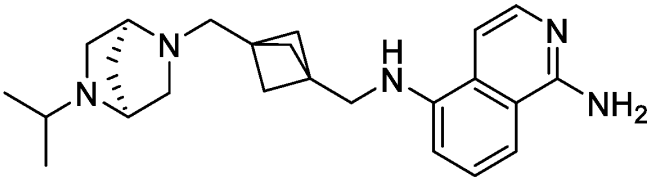
in DCM) and further purified by automated prep HPLC (mass directed 2-60% MeCN in water with a basic mobile phase of 0.1% NH_3 in water over 20 min) and lyophillised to afford the product (15 mg, 40% yield).

$[M+H]^+ = 375.2$

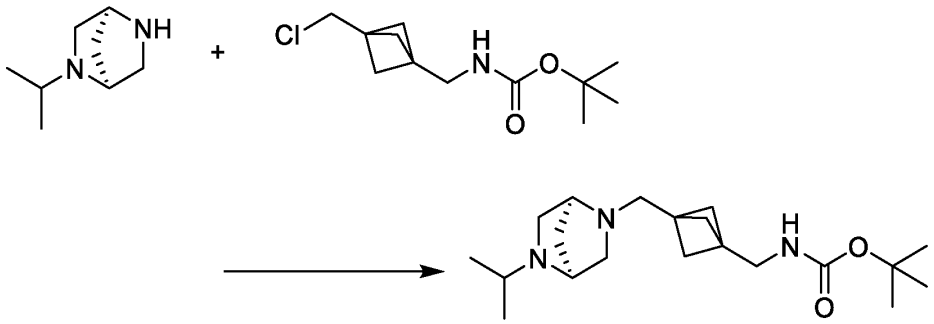
^1H NMR (DMSO-d6, 400 MHz) δ 1.69 (6H, s), 2.56 (2H, s), 2.80 (2H, dd, J = 6.3, 4.7 Hz), 3.28 (2H, d, J = 5.6 Hz), 3.56 (2H, s), 3.91 (2H, t, J = 5.5 Hz), 5.81 (1H, t, J = 5.9 Hz), 6.47 (2H, s), 6.63 (1H, d, J = 7.6 Hz), 6.80 (1H, d, J = 1.2 Hz), 7.00 (1H, d, J = 1.2 Hz), 7.13 (1H, d, J = 6.1 Hz), 7.19 (1H, t, J = 8.0 Hz), 7.30 (1H, d, J = 8.3 Hz), 7.70 (1H, d, J = 6.1 Hz) ppm.

Example number 1005.1

N5-((3-(((1S,4S)-5-Isopropyl-2,5-diazabicyclo[2.2.1]heptan-2-yl)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine



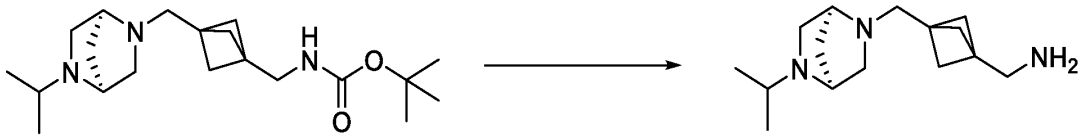
Tert-butyl N-[[3-[[(1S,4S)-5-propan-2-yl-2,5-diazabicyclo[2.2.1]heptan-2-yl]methyl]-1-bicyclo[1.1.1]pentanyl]methyl]carbamate



Following General Method **2b**, (1S,4S)-2-(propan-2-yl)-2,5-diazabicyclo[2.2.1]heptane (51 mg, 0.37 mmol) was reacted with tert-butyl N-[[3-(chloromethyl)-1-bicyclo[1.1.1]pentanyl]methyl]carbamate (90 mg, 0.37 mmol) and K_2CO_3 (103 mg, 0.73 mmol) in MeCN (5 mL) at 60 °C for 72 h. The reaction was diluted with water (20 mL) and the aqueous was extracted with DCM (3 x 20 mL). The combined organics were washed with brine (20 mL), dried ($MgSO_4$), filtered and concentrated to afford the product (128 mg, 100% yield).

$[M+H]^+ = 350.1$

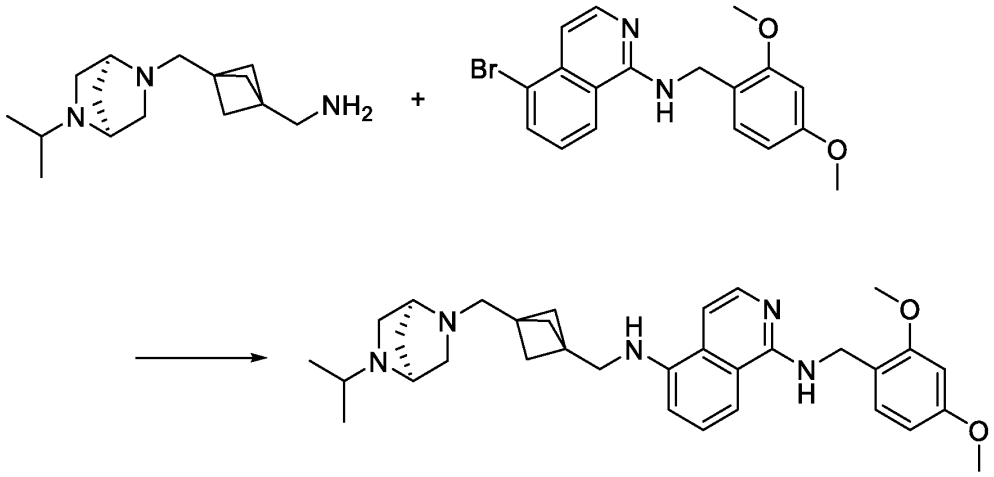
[3-[[(1S,4S)-5-propan-2-yl-2,5-diazabicyclo[2.2.1]heptan-2-yl]methyl]-1-bicyclo[1.1.1]pentanyl]methanamine



tert-Butyl N-[[3-[[(1S,4S)-5-propan-2-yl-2,5-diazabicyclo[2.2.1]heptan-2-yl]methyl]-1-bicyclo[1.1.1]pentanyl]methyl]carbamate (128 mg , 0.37 mmol) was deprotected according to General Method **5a**, in 1,4-dioxane (4 mL) with 4M HCl in dioxane (916 µL, 3.66 mmol). The reaction was stirred at rt for 20 h and then concentrated. The free base of the resulting HCl salt was liberated by dissolving in MeOH and passing through PL-HCO_3 MP SPE (Agilent). The solvent was removed *in vacuo* to afford the product (91 mg, 100% yield).

$[M+H]^+$ = 250.2

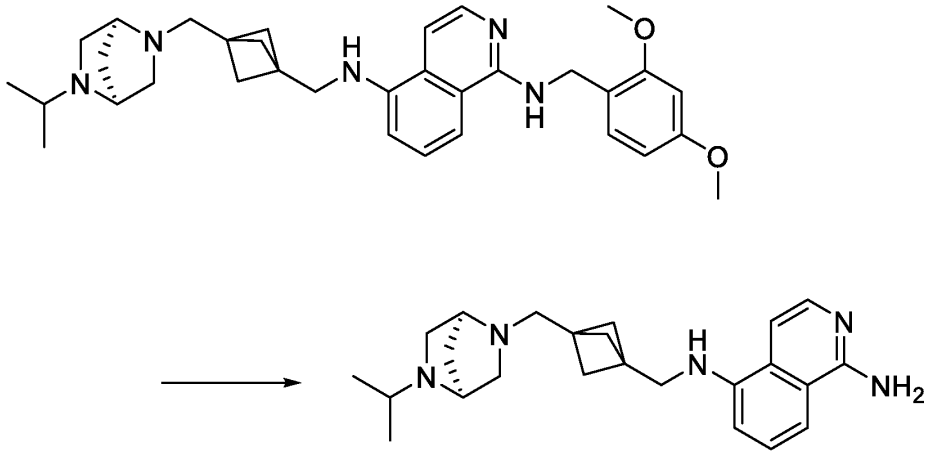
1-N-[(2,4-dimethoxyphenyl)methyl]-5-N-[[3-[[(1S,4S)-5-propan-2-yl-2,5-diazabicyclo[2.2.1]heptan-2-yl]methyl]-1-bicyclo[1.1.1]pentanyl]methyl]isoquinoline-1,5-diamine



Using General Method **4**, 5-bromo-N-[(2,4-dimethoxyphenyl)methyl]isoquinolin-1-amine (136 mg, 0.36 mmol) was reacted with [3-[[(1S,4S)-5-propan-2-yl-2,5-diazabicyclo[2.2.1]heptan-2-yl]methyl]-1-bicyclo[1.1.1]pentanyl]methanamine (91 mg , 0.36 mmol) in the presence of Cs_2CO_3 (239 mg, 0.73 mmol) and Brettphos Pd G4 (33 mg , 0.04 mmol) in 1,4-dioxane (5 mL) in a sealed vial at 60 °C for 72 h. The reaction was cooled to rt and filtered through Celite®. The crude product was purified by flash chromatography (SNAP KP-NH (Biotage®), 0-20% MeOH in DCM) to afford the product (100 mg, 51% yield).

$[M+H]^+$ = 542.4

N5-((3-(((1S,4S)-5-isopropyl-2,5-diazabicyclo[2.2.1]heptan-2-yl)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine (Example 1005.1)



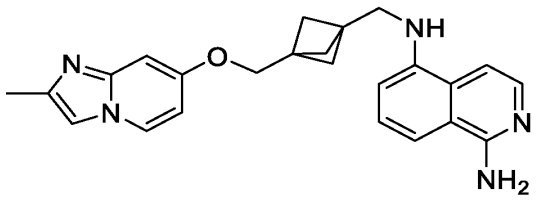
1-N-[(2,4-Dimethoxyphenyl)methyl]-5-N-[[3-[[(1S,4S)-5-propan-2-yl-2,5-diazabicyclo[2.2.1]heptan-2-yl]methyl]-1-bicyclo[1.1.1]pentanyl]methyl]isoquinoline-1,5-diamine (101 mg , 0.19 mmol) was deprotected using General Method **8**. The reaction mixture was cooled to rt and the solvent was removed , azeoptroping with toluene (10 mL). The crude product was purified by SCX, followed by automated prep HPLC (mass directed 2-60% MeCN in water with a basic mobile phase of 0.1% NH_3 in water over 20 min) and lyophillised to afford the product (34 mg, 47% yield).

$[M+H]^+$ = 392.2

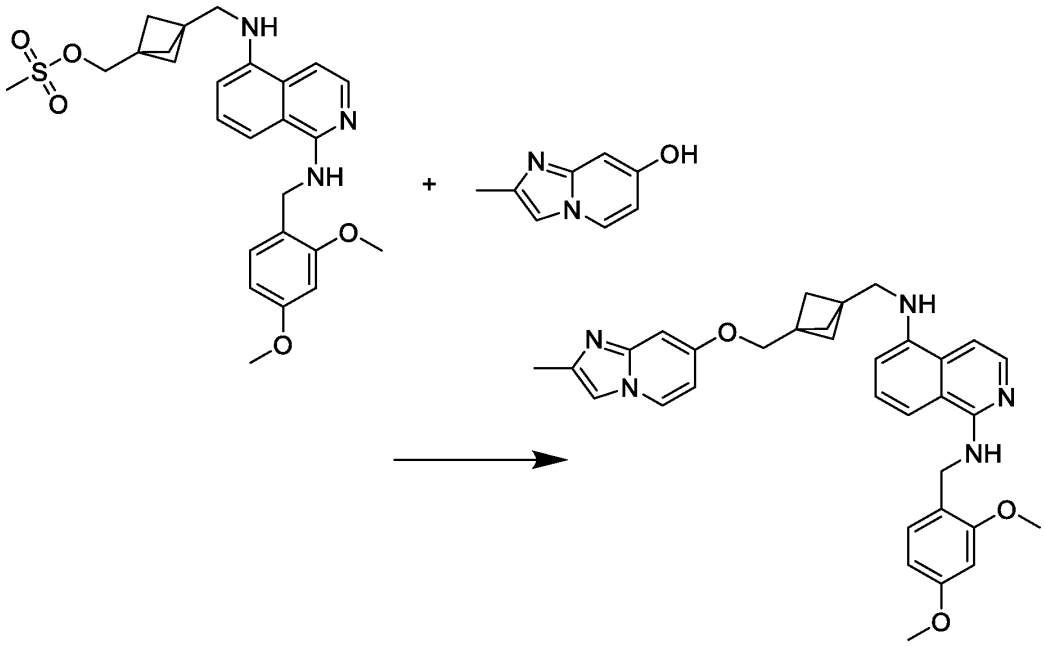
^{1}H NMR (DMSO-d6, 400 MHz) δ 0.89 (3H, d, J = 6.1 Hz), 0.94 (3H, d, J = 6.0 Hz), 1.45 (1H, d, J = 9.0 Hz), 1.51 (1H, d, J = 9.0 Hz), 1.58 (6H, s), 2.36 - 2.40 (1H, m), 2.41 (1H, d, J = 7.9 Hz), 2.46 - 2.49 (1H, m), 2.51 - 2.53 (2H, m), 2.55 (2H, d, J = 9.9 Hz), 2.68 (1H, dd, J = 9.3, 2.6 Hz), 3.13 (1H, s), 3.27 (2H, d, J = 5.7 Hz), 5.80 (1H, t, J = 5.8 Hz), 6.48 (2H, s), 6.61 (1H, d, J = 7.7 Hz), 7.09 - 7.15 (1H, m), 7.18 (1H, t, J = 8.0 Hz), 7.30 (1H, d, J = 8.3 Hz), 7.70 (1H, d, J = 6.0 Hz)

Example number 1006

N5-((3-(((2-Methylimidazo[1,2-a]pyridin-7-yl)oxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine

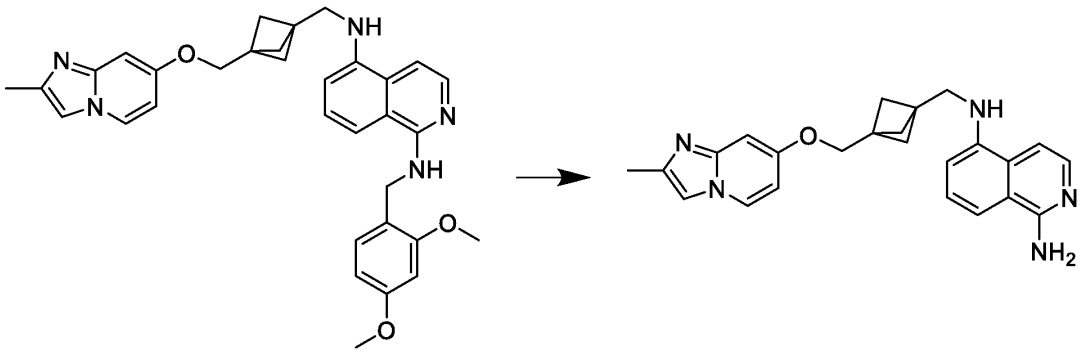


1-N-[(2,4-Dimethoxyphenyl)methyl]-5-N-[[3-[(2-methylimidazo[1,2-a]pyridin-7-yl)oxymethyl]-1-bicyclo[1.1.1]pentanyl]methyl]isoquinoline-1,5-diamine



Following General Method **2b** [3-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-1-bicyclo[1.1.1]pentanyl]methyl methanesulfonate (120 mg, 0.24 mmol) was reacted with 2-methylimidazo[1,2-a]pyridin-7-ol (39 mg, 0.26 mmol) and K_2CO_3 (146 mg, 1.05 mmol) in MeCN (3 mL) at 60 °C for 72 h. The mixture was diluted with water (5 mL). The aqueous was extracted with DCM (3 x 10 mL). The combined organics were washed with brine, dried ($MgSO_4$) and concentrated. Flash chromatography (Silica, 0-20% (10% NH_4OH in MeOH) in DCM) afforded the product (31 mg, 23% yield). $[M+H]^+ = 550.1$

N5-((3-(((2-Methylimidazo[1,2-a]pyridin-7-yl)oxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine (Example 1006)



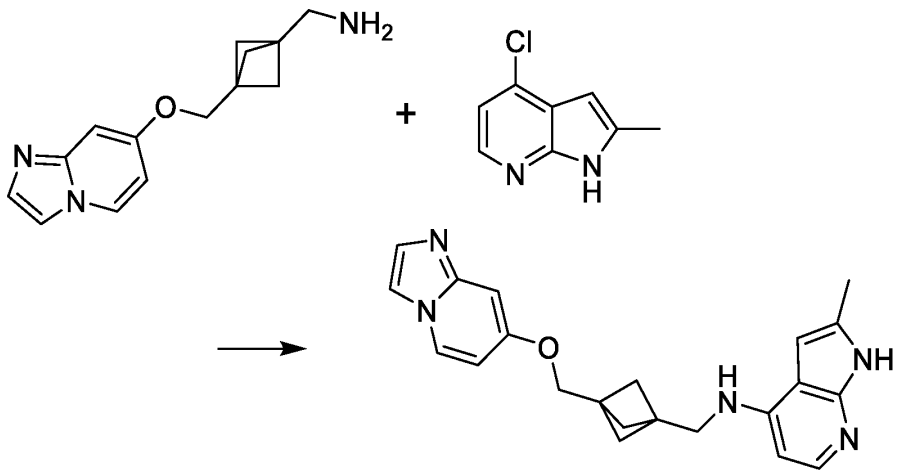
1-N-[(2,4-Dimethoxyphenyl)methyl]-5-N-[[3-[(2-methylimidazo[1,2-a]pyridin-7-yl)oxymethyl]-1-bicyclo[1.1.1]pentanyl]methyl]isoquinoline-1,5-diamine (31 mg, 0.06 mmol) was deprotected according to General Method **8**, in TFA (6 mg, 0.06 mmol) at 50 °C for 30 min. The solvent was removed *in vacuo*, azeoptroping with toluene (20 mL). The residue was dissolved in MeOH (3 mL), filtered and passed through SCX-2 and washed with MeOH (3 x 5 mL). The required compound was eluted with a solution of 1M NH_3 in MeOH (3 x 5 mL) and the solvent was removed. Flash chromatography (Silica, 0-20% (10% NH_4OH in MeOH) in DCM) afforded the product (6 mg, 25% yield).

$[M+H]^+$ = 400.2

^1H NMR (CD_3CN, 400 MHz) δ 1.83 (6H, s), 2.31 (3H, d, J = 0.9 Hz), 3.40 (2H, d, J = 4.1 Hz), 4.06 (2H, s), 4.86 (1H, s), 5.57 (2H, s), 6.46 (1H, dd, J = 7.4, 2.5 Hz), 6.72 (1H, d, J = 2.5 Hz), 6.77 - 6.81 (1H, m), 7.05 (1H, dd, J = 6.1, 1.0 Hz), 7.20 (1H, dt, J = 8.3, 1.0 Hz), 7.30 (1H, s), 7.34 (1H, t, J = 8.0 Hz), 7.83 (1H, d, J = 6.2 Hz), 8.03 (1H, dd, J = 7.4, 0.7 Hz) ppm.

Example number 1012

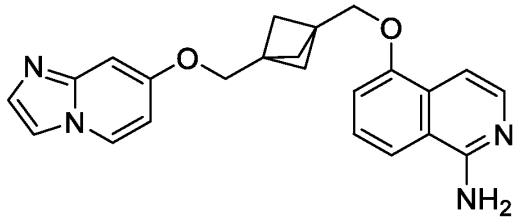
N-((3-((Imidazo[1,2-a]pyridin-7-yloxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)-2-methyl-1H-pyrrolo[2,3-b]pyridin-4-amine



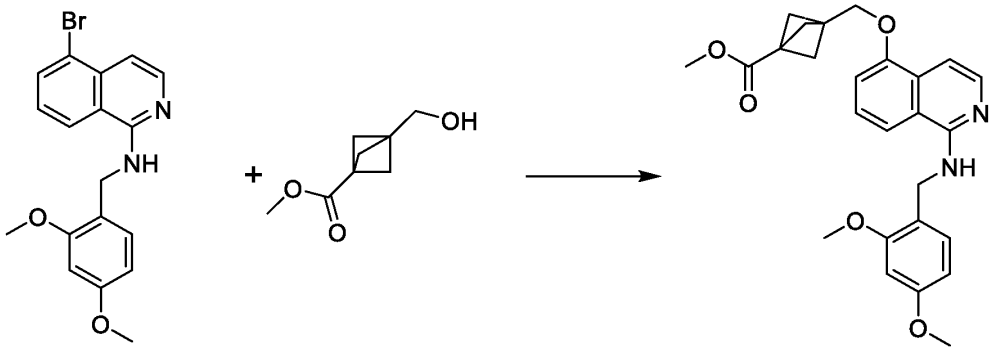
According to General Method **4**, (3-((imidazo[1,2-a]pyridin-7-yloxy)methyl)bicyclo[1.1.1]pentan-1-yl)methanamine (233 µmol) and 4-chloro-2-methyl-1H-pyrrolo[2,3-b]pyridine (228 µmol) were reacted in the presence of BrettPhos Pd G3 (11.4 µmol) and LiHMDS (547 µmol). The reaction was quenched with AcOH. The crude product was purified by an SCX eluting with NH_3 in MeOH followed by purification by flash chromatography (Silica, 0-6% (0.7M NH_3 in MeOH) in DCM) then re-purified by flash chromatography (Silica, 0-9% (0.7M NH_3 in MeOH) in EtOAc). Product was further purified by automated prep HPLC (mass directed MeCN 15-45% in water over 12.5 min in basic mobile phase) to obtain the product (18 mg, 21%).
[M+H] = 374.3
^{1}H NMR (500 MHz, DMSO-d6) δ 1.72 (6H, s), 2.29 (3H, s), 3.32 (2H, s, obscured by H_2O), 4.03 (2H, s), 6.08 (1H, d, J = 5.5 Hz), 6.16 - 6.26 (2H, m), 6.56 (1H, dd, J = 7.4, 2.5 Hz), 6.86 (1H, d, J = 2.5 Hz), 7.36 (1H, s), 7.67 (1H, d, J = 5.5 Hz), 7.71 (1H, s), 8.35 (1H, d, J = 7.4 Hz), 10.89 (1H, s).

Example number 1013

5-[[3-(Imidazo[1,2-a]pyridin-7-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methoxy]isoquinolin-1-amine



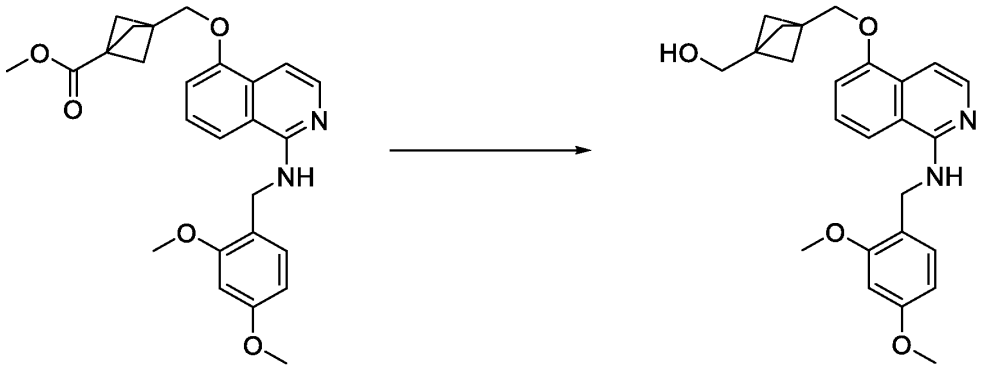
Methyl 3-[[1-[(2,4-dimethoxyphenyl)methylamino]-5-isoquinolyl]oxymethyl]bicyclo[1.1.1]pentane-1-carboxylate



According to General Method **4**, 5-bromo-N-[(2,4-dimethoxyphenyl)methyl]isoquinolin-1-amine (478 mg, 1.28 mmol) and methyl 3-(hydroxymethyl)bicyclo[1.1.1]pentane-1-carboxylate (200 mg, 1.28 mmol) were reacted in the presence of Cs_2CO_3 (2099 mg, 6.4 mmol) and Brettphos Pd G4 (147 mg, 0.16 mmol) in 1,4-dioxane (10 mL) at 90 °C in a sealed vial for 3 days. Purification by flash chromatography (silica, 0 - 80% EtOAc in Pet. Ether) afforded the product (230 mg, 40% yield).

$[M+H]^+$ = 449.2

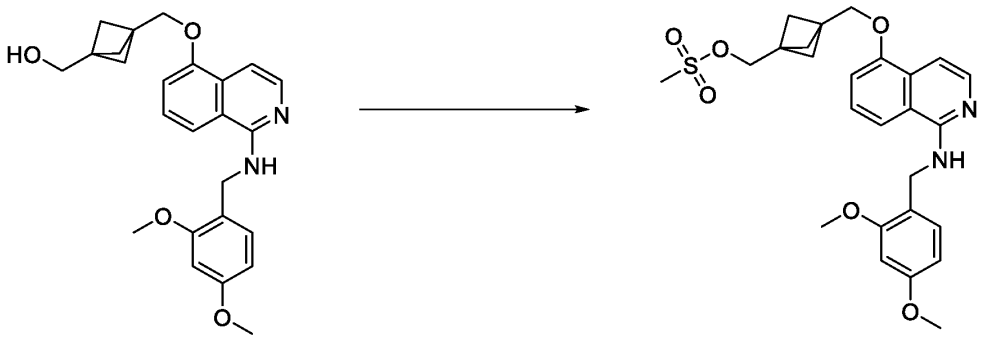
[3-[[1-[(2,4-Dimethoxyphenyl)methylamino]isoquinolin-5-yl]oxymethyl]-1-bicyclo[1.1.1]pentanyl]methanol



According to General Method **3b**, methyl 3-[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]oxymethyl]bicyclo[1.1.1]pentane-1-carboxylate (230 mg, 0.51 mmol) was reacted with $LiAlH_4$ to afford the product (215 mg, 100% yield).

$[M+H]^+$ = 421.2

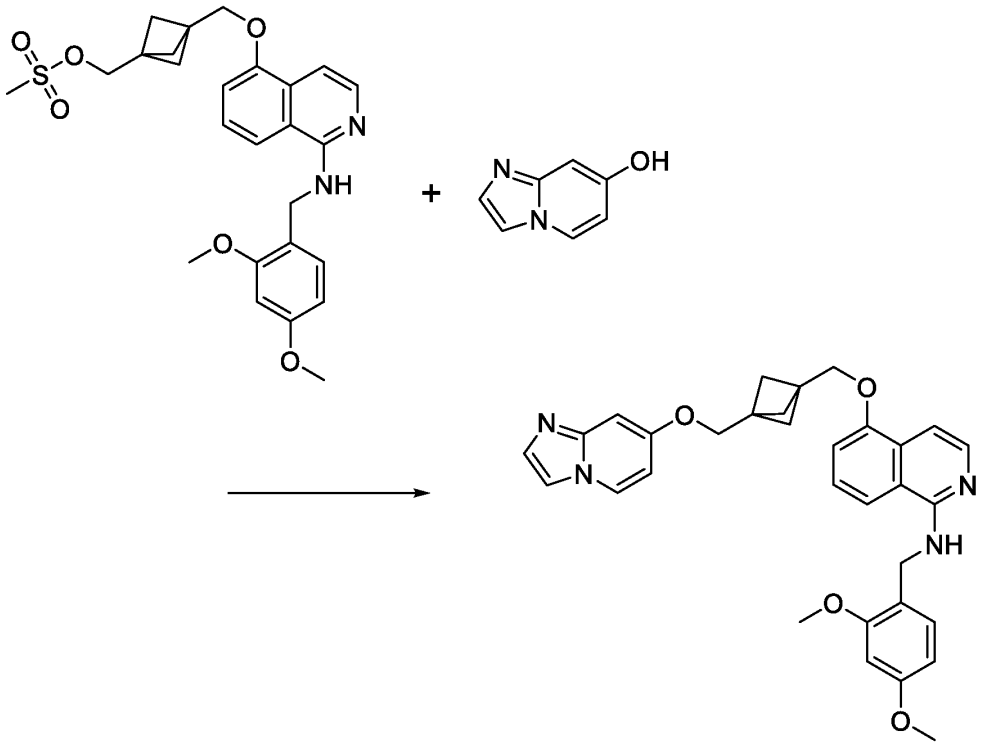
[3-[[1-[(2,4-Dimethoxyphenyl)methylamino]isoquinolin-5-yl]oxymethyl]-1-bicyclo[1.1.1]pentanyl]methyl methanesulfonate



According to General Method **1a,** [3-[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]oxymethyl]-1-bicyclo[1.1.1]pentanyl]methanol (105 mg, 0.25 mmol) was reacted with methane sulfonyl chloride (23 µL, 0.3 mmol) to obtain the product (120 mg, 87% yield) which was used without purification.

$[M+H]^+$ = 499.2

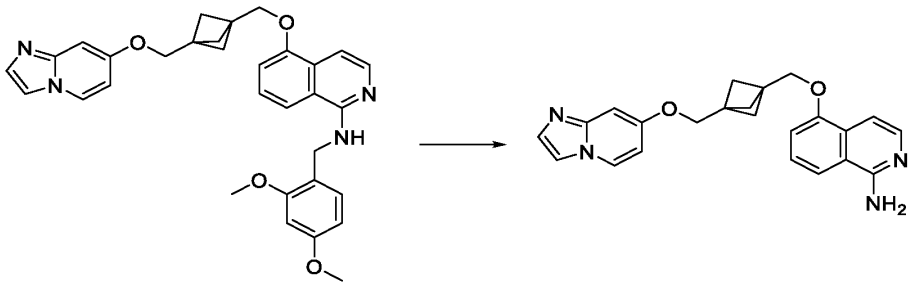
N-[(2,4-Dimethoxyphenyl)methyl]-5-[[3-(imidazo[1,2-a]pyridin-7-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methoxy]isoquinolin-1-amine



According to General Method **2a**, imidazo[1,2-a]pyridin-7-ol hydrochloride (37 mg, 0.22 mmol) was reacted with [3-[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]oxymethyl]-1-bicyclo[1.1.1]pentanyl]methyl methanesulfonate (120 mg, 0.22 mmol). Purification by flash chromatography (silica, 0 - 100% (3:3:1 EtOAc:MeCN:EtOH + 2% NH_4OH) in Pet. Ether) afforded the product (23 mg, 18% yield).

$[M+H]^+ = 537$

5-[[3-(Imidazo[1,2-a]pyridin-7-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methoxy]isoquinolin-1-amine (Example 1013)



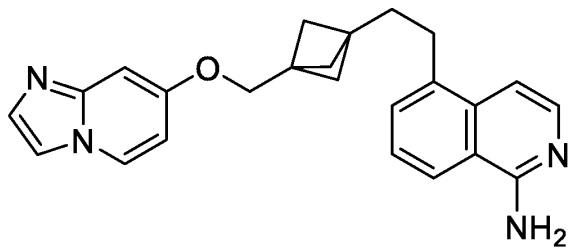
N-[(2,4-Dimethoxyphenyl)methyl]-5-[[3-(imidazo[1,2-a]pyridin-7-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methoxy]isoquinolin-1-amine (23 mg, 0.04 mmol) was reacted according to General Method **8** and purified by automated prep HPLC (mass directed 2-60% MeCN in water with a basic mobile phase of 0.1% NH_3 in water over 20 min) and lyophilized to afford the product (8 mg, 48% yield).

$[M+H]^+ = 387.2$

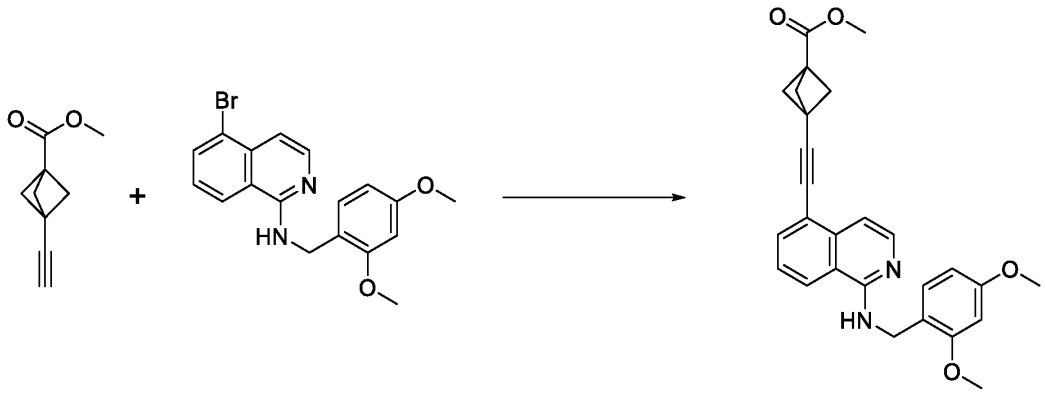
^1H NMR (DMSO-d_6, 400 MHz) δ 1.88 (6H, s), 4.12 (2H, s), 4.16 (2H, s), 6.63 (1H, dd, J = 7.4, 2.4 Hz), 6.76 (2H, s), 6.92 (1H, d, J = 2.3 Hz), 7.07 (1H, d, J = 7.7 Hz), 7.13 (1H, d, J = 5.8 Hz), 7.35 (1H, t, J = 8.1 Hz), 7.38 (1H, d, J = 0.6 Hz), 7.70 - 7.74 (2H, m), 7.80 (1H, d, J = 5.9 Hz), 8.38 (1H, d, J = 7.4 Hz

Example number 1014

5-[2-[3-Imidazo[1,2-a]pyridin-7-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]ethyl]isoquinolin-1-amine



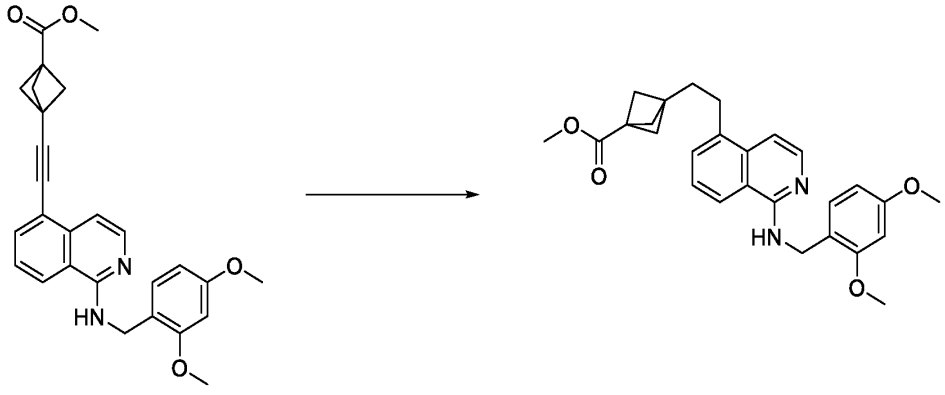
Methyl 3-[2-[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]ethynyl]bicyclo[1.1.1]pentane-1-carboxylate



To a sealed vial which had been flushed with N_2 was added 5-bromo-N-[(2,4-dimethoxyphenyl)methyl]isoquinolin-1-amine (255 mg, 0.68 mmol), CuI (38 mg, 0.2 mmol) and $Pd(PPh_3)_4$ (77 mg, 0.07 mmol). TEA (186 µL, 1.33 mmol) and 1,4-dioxane (5 mL) were added and the mixture was purged with N_2 while stirring for 10 min. Methyl 3-ethynylbicyclo[1.1.1]pentane-1-carboxylate (100 mg, 0.67 mmol) was added and the mixture was stirred at 50 °C for 2 days. The mixture was filtered through Celite®, washed with EtOAc and concentrated. Flash chromatography (Silica, 0-60% EtOAc in Pet. Ether) afforded the product (182 mg, 62% yield).

$[M+H]^+ = 443.2$

Methyl 3-[2-[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]ethyl]bicyclo[1.1.1]pentane-1-carboxylate

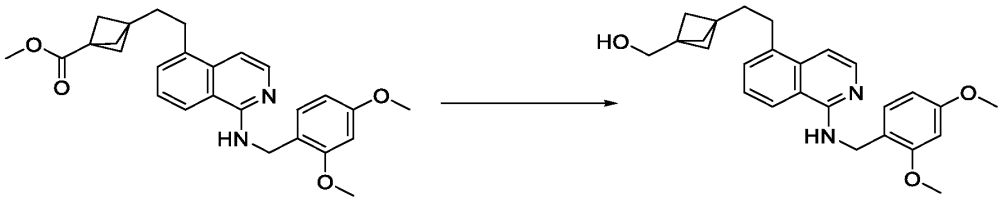


Reduction of methyl 3-[2-[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]ethynyl]bicyclo[1.1.1]pentane-1-carboxylate (182 mg, 0.41 mmol) was performed using General

Method **3a** in a solution of ethanol (20 mL) at rt, 1 bar and a flow rate of 1 mL/min using a 10% Pd/C CatCart. The solvent was removed to afford the product (166 mg, 90% yield).

$[M+H]^+$ = 447.2

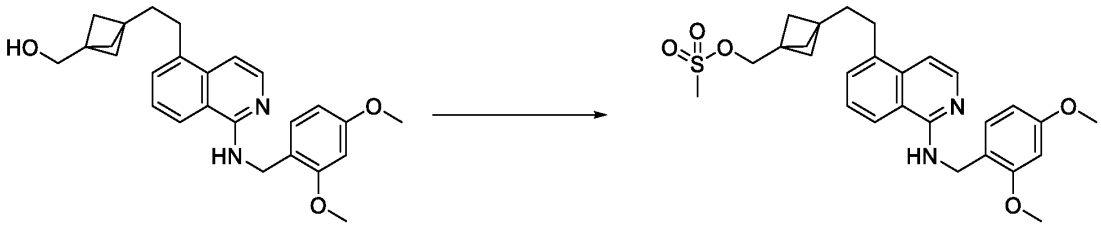
[3-[2-[1-[(2,4-Dimethoxyphenyl)methylamino]isoquinolin-5-yl]ethyl]-1-bicyclo[1.1.1]pentanyl]methanol



Using General Method **3b**, reduction of methyl 3-[2-[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]ethyl]bicyclo[1.1.1]pentane-1-carboxylate (166 mg, 0.37 mmol) was carried out over 1 hour. The reaction was diluted with Et_2O and cooled in an ice/water bath before water (0.1 mL) was added, followed by 2M NaOH (aq) (0.1 mL), and water (0.3 mL). The mixture was stirred at rt for 15 min before adding Na_2SO_4. The mixture was stirred for a further 15 min, filtered and concentrated to afford the product (154 mg, 99% yield).

$[M+H]^+$ = 419.2

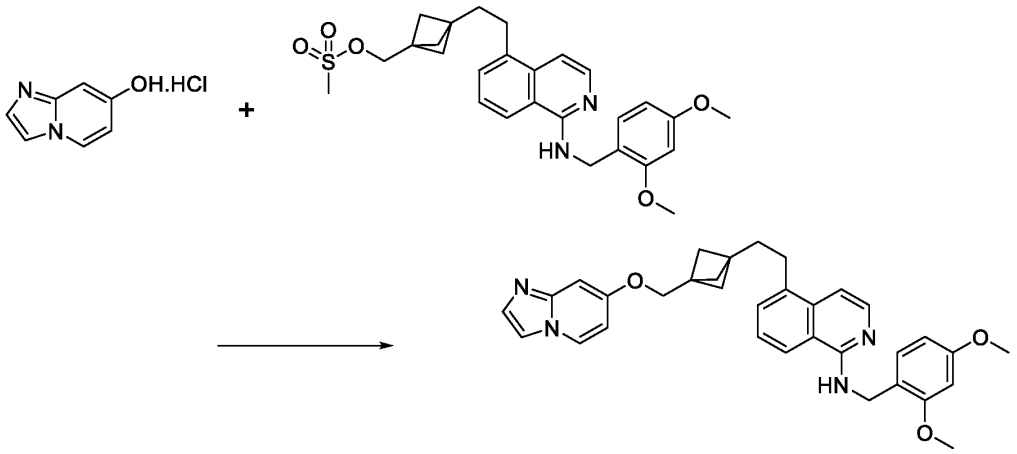
[3-[2-[1-[(2,4-Dimethoxyphenyl)methylamino]isoquinolin-5-yl]ethyl]-1-bicyclo[1.1.1]pentanyl]methyl methanesulfonate



Following General Method **1a**, [3-[2-[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]ethyl]-1-bicyclo[1.1.1]pentanyl]methanol (154 mg, 0.37 mmol) was reacted with methane sulfonyl chloride (34 µL, 0.44 mmol) while cooling in an ice/water bath for 90 min to afford the product (183 mg, 100% yield) which was used without purification by flash chromatography.

$[M+H]^+$ = 497.2

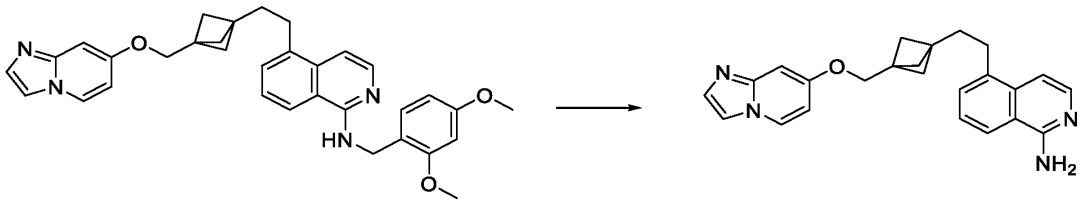
N-[(2,4-Dimethoxyphenyl)methyl]-5-[2-[3-(imidazo[1,2-a]pyridin-7-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]ethyl]isoquinolin-1-amine



3-[2-[1-[(2,4-Dimethoxyphenyl)methylamino]isoquinolin-5-yl]ethyl]-1-bicyclo[1.1.1]pentanyl]methyl methanesulfonate (100 mg, 0.2 mmol) and imidazo[1,2-a]pyridin-7-ol hydrochloride (34 mg, 0.2 mmol) were taken up in DMF (5 mL) and TEA (28 µL, 0.2 mmol). The mixture was cooled in an ice/water bath and NaH (60% dispersion in mineral oil) (16 mg, 0.4 mmol) was added. The reaction mixture was heated to 50 °C overnight. DCM (30 mL) and water (10 mL) were added. The layers were separated and the aqueous layer was back-extracted with DCM (3 x 10 mL). The organic layers were combined, dried ($MgSO_4$) and concentrated. Flash chromatography (silica, 0-100% EtOAc in Pet. Ether followed by 0 - 20% MeOH in DCM) afforded the product (29 mg, 27% yield).

$[M+H]^+$ = 535.3

5-[2-[3-(Imidazo[1,2-a]pyridin -7-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]ethyl]isoquinolin-1-amine (Example 1014)



N-[(2,4-Dimethoxyphenyl)methyl]-5-[2-[3-(imidazo[1,2-a]pyridin-7-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]ethyl]isoquinolin-1-amine (29 mg, 0.05 mmol) was reacted according to General Method **8** and purified by automated prep HPLC (mass directed 2-60% MeCN in water with a basic mobile phase of 0.1% NH_3 in water over 20 min) and lyophilised to afford the product (29 mg, 26% yield). Analysis indicated the presence of alkene side product carried over from the palladium catalysed hydrogenation of the alkyne. This mixture (14 mg, 0.04 mmol) was taken up in EtOH (5 mL) and subjected to

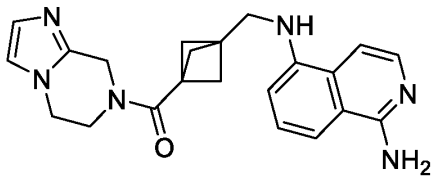
hydrogenation in the H-Cube® using 10% Pd/C at rt, 1 bar, flow rate 1 mL/min. The mixture was concentrated and lyophilised to afford the product (7 mg, 50% yield).

$[M+H]^+$ = 385.2

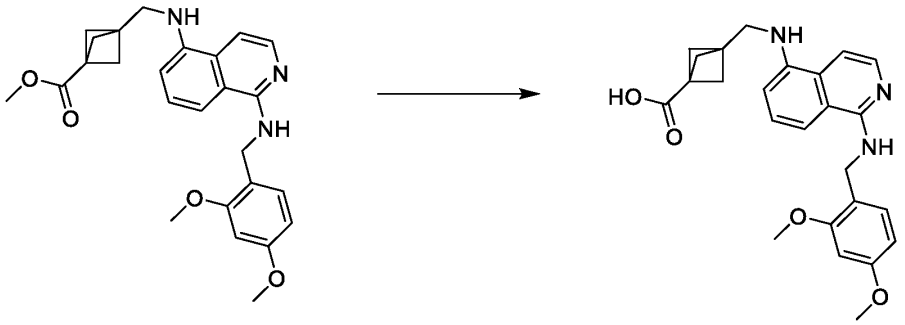
^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.78 (6H, s), 1.86 - 1.97 (2H, m), 2.90 - 2.99 (2H, m), 4.02 (2H, s), 5.28 (2H, d, J = 18.4 Hz), 6.53 (1H, dd, J = 7.4, 2.4 Hz), 6.84 (1H, d, J = 2.5 Hz), 7.15 (1H, dd, J = 6.2, 1.0 Hz), 7.36 - 7.45 (2H, m), 7.48 (2H, dd, J = 7.2, 1.3 Hz), 7.68 (1H, dt, J = 8.3, 1.3 Hz), 7.93 (1H, dd, J = 7.4, 0.7 Hz), 7.96 (1H, d, J = 6.2 Hz)

Example number 1016

[3-[[(1-Aminoisoquinolin-5-yl)amino]methyl]-1-bicyclo[1.1.1]pentanyl]-(6,8-dihydro-5H-imidazo[1,2-a]pyrazin-7-yl)methanone



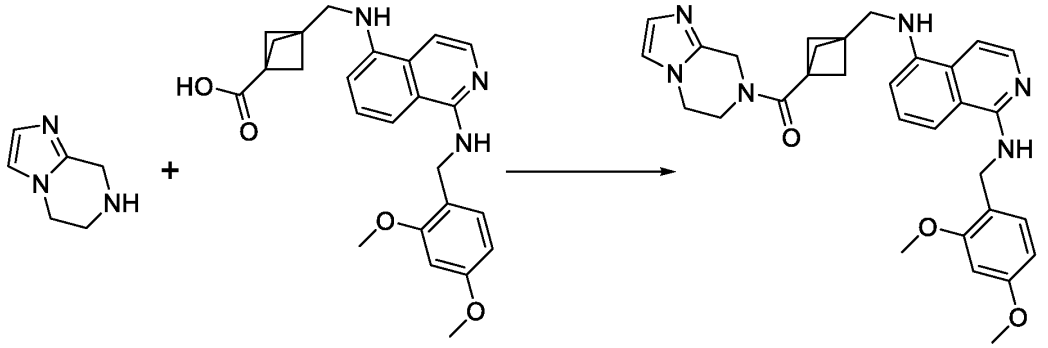
3-[[[1-[(2,4-Dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]bicyclo[1.1.1]pentane-1-carboxylic acid



To a solution of methyl 3-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]bicyclo[1.1.1]pentane-1-carboxylate (100 mg, 0.22 mmol) in THF (4 mL) and water (1 mL) was added lithium hydroxide monohydrate (64 mg, 1.11 mmol) and the reaction stirred at 50 °C for 3 h. The mixture was cooled to rt and concentrated. The crude residue was partitioned between water and $CHCl_3$. The aqueous layer was acidified to pH 1 with 2N HCl (aq) and the product extracted into isopropanol:$CHCl_3$ (1:3) (5 x 10 mL). The combined organic layers from the acid work-up were dried ($MgSO_4$), filtered and concentrated to afford the product (80 mg, 83% yield).

$[M+H]^+$ = 434.2

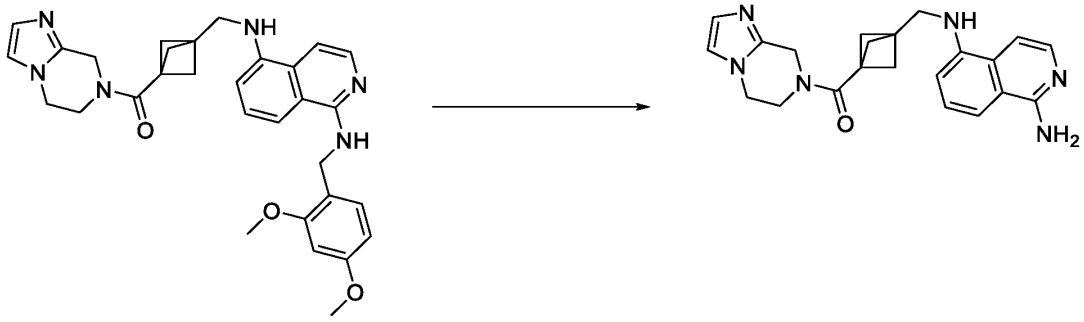
6,8-Dihydro-5H-imidazo[1,2-a]pyrazin-7-yl-[3-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-1-bicyclo[1.1.1]pentanyl]methanone



5,6,7,8-Tetrahydroimidazo[1,2-a]pyrazine (23 mg, 0.18 mmol) and 3-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]bicyclo[1.1.1]pentane-1-carboxylic acid (80 mg, 0.18 mmol) were taken up in DCM (10 mL) and cooled in an ice/water bath. HOBt (34 mg, 0.22 mmol), TEA (129 uL, 0.92 mmol) and EDC (50 mg, 0.26 mmol) were added and the mixture stirred at rt for 6 days. The mixture was diluted with DCM (25 mL) and sat. $NaHCO_3$ (aq) 10 mL). The aqueous layer was re-extracted into DCM (25 mL) and the combined organic layers were dried ($MgSO_4$), filtered and concentrated. Flash chromatography (Silica, 0-20% MeOH in DCM) afforded the product (50 mg, 50% yield).

$[M+H]^+$ = 539.3

[3-[[(1-Aminoisoquinolin-5-yl)amino]methyl]-1-bicyclo[1.1.1]pentanyl]-(6,8-dihydro-5H-imidazo[1,2-a]pyrazin-7-yl)methanone (Example 1016)



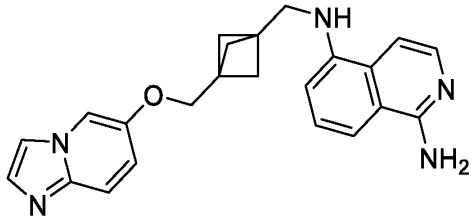
6,8-Dihydro-5H-imidazo[1,2-a]pyrazin-7-yl-[3-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-1-bicyclo[1.1.1]pentanyl]methanone (50 mg, 0.09 mmol) was deprotected according to General Method **8** in DCM (1 mL). Following SCX the resulting residue was lyophilized to afford the product (35 mg, 97% yield).

$[M+H]^+$ = 389.2

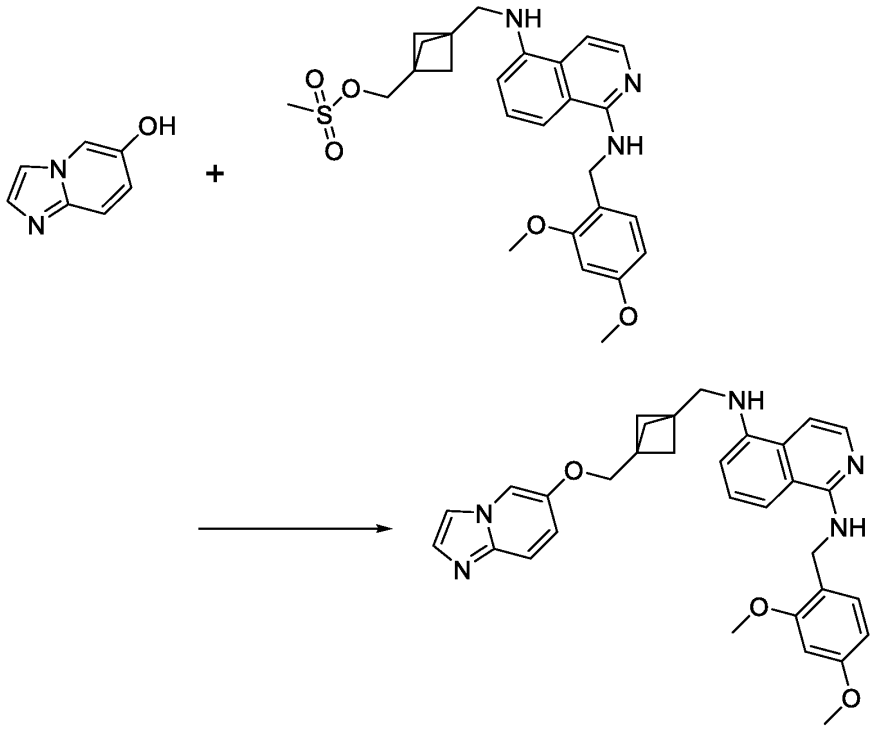
^{1}H NMR (DMSO-d6, 400 MHz) δ 2.08 (6H, s), 2.95 - 3.20 (1H, m), 3.81 - 4.05 (5H, m), 4.58 - 4.79 (2H, m), 5.86 - 5.93 (1H, m), 6.52 (2H, s), 6.65 (1H, d, J = 7.7 Hz), 6.87 (1H, d, J = 9.3 Hz), 7.09 - 7.23 (3H, m), 7.33 (1H, d, J = 8.3 Hz), 7.72 (1H, d, J = 6.2 Hz)

Example number 1017

5-N-[[3-(Imidazo[1,2-a]pyridin-6-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methyl]isoquinoline-1,5-diamine



1-N-[(2,4-Dimethoxyphenyl)methyl]-5-N-[[3-(imidazo[1,2-a]pyridin-6-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methyl]isoquinoline-1,5-diamine

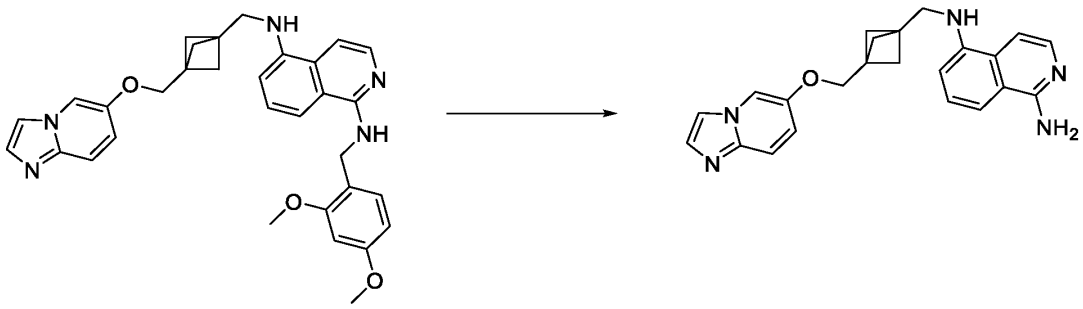


Following General Method **2b**, [3-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-1-bicyclo[1.1.1]pentanyl]methyl methanesulfonate (150 mg, 0.3 mmol) was reacted with imidazo[1,2-a]pyridin-6-ol (61 mg, 0.45 mmol) and K_2CO_3 (167 mg, 1.21 mmol) in MeCN (5 mL) at 90

°C for 3 days. Purification by flash chromatography (Silica, 0 - 20% (10% NH_3 in MeOH) in DCM) afforded the product (80 mg, 45% yield).

$[M+H]^+$ = 536.3

5-N-[[3-(Imidazo[1,2-a]pyridin-6-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methyl]isoquinoline-1,5-diamine (Example 1017)



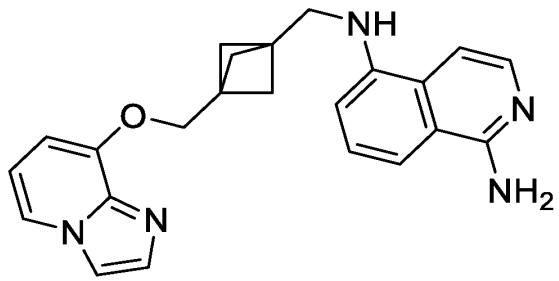
1-N-[(2,4-Dimethoxyphenyl)methyl]-5-N-[[3-(imidazo[1,2-a]pyridin-6-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methyl]isoquinoline-1,5-diamine (19 mg, 0.04 mmol) was deprotected according to General Method **8**. After SCX, lyophilisation afforded the product (13 mg, 92% yield).

$[M+H]^+$ = 386.2

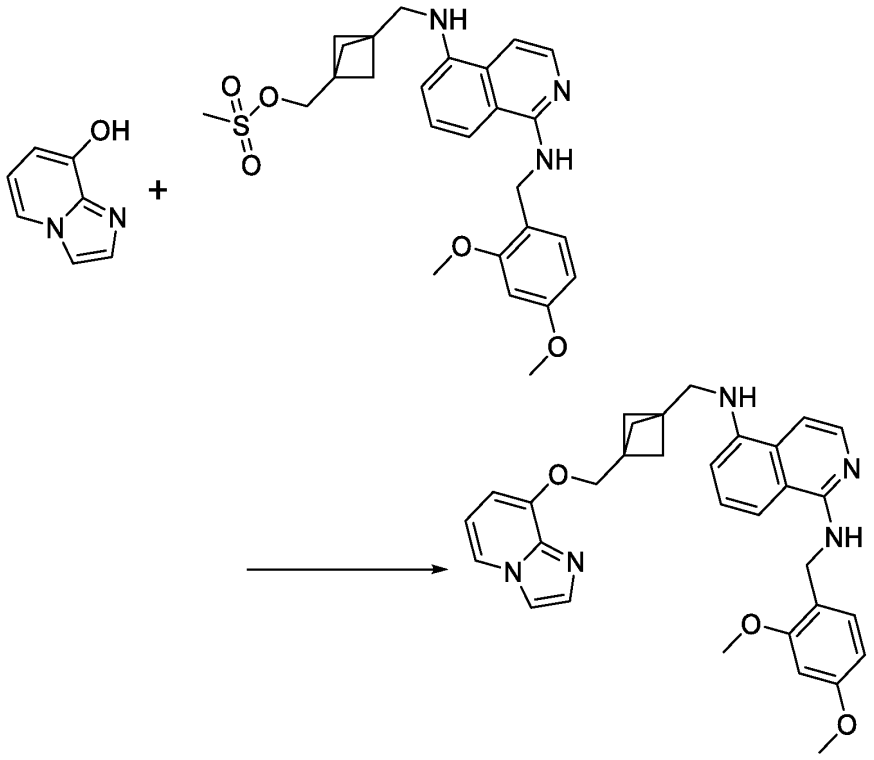
^1H NMR (DMSO-d6, 400 MHz) δ 1.75 (6H, s), 3.96 (2H, s), 5.92 (1H, t, J = 6.0 Hz), 6.62 (2H, s), 6.67 (1H, d, J = 7.7 Hz), 6.99 (1H, dd, J = 9.8, 2.4 Hz), 7.16 (1H, d, J = 6.2 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.44 (1H, d, J = 9.7 Hz), 7.48 (1H, d, J = 1.2 Hz), 7.70 (1H, d, J = 6.2 Hz), 7.79 (1H, s), 8.23 (1H, d, J = 2.4 Hz). 2H masked by water peak (confirmed by COSY)

Example number 1018

5-N-[[3-(Imidazo[1,2-a]pyridin-8-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methyl]isoquinoline-1,5-diamine



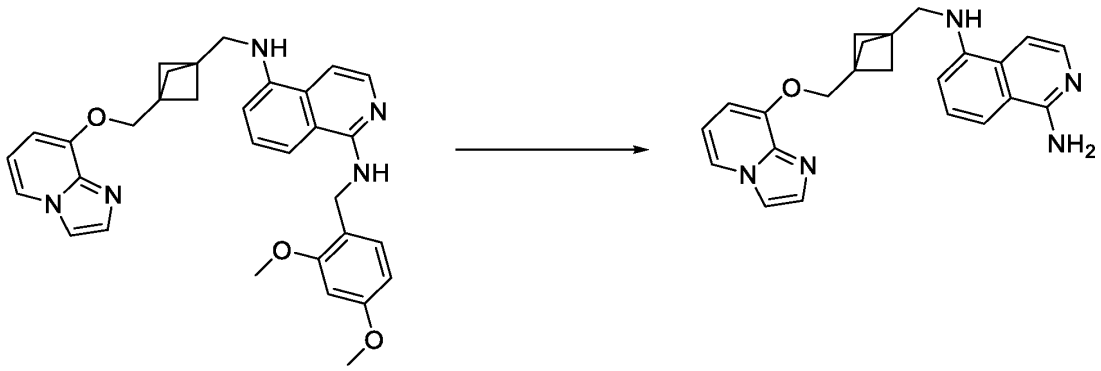
1-N-[(2,4-Dimethoxyphenyl)methyl]-5-N-[[3-(imidazo[1,2-a]pyridin-8-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methyl]isoquinoline-1,5-diamine



Following General Method **2b**, [3-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-1-bicyclo[1.1.1]pentanyl]methyl methanesulfonate (70 mg, 0.14 mmol) was reacted with imidazo[1,2-a]pyridin-8-ol (28 mg, 0.21 mmol) and K_2CO_3 (78 mg, 0.56 mmol) in MeCN (3 mL) under microwave heating at 120 °C for 90 min. After work up the crude material was purified by flash chromatography (Silica, 0 - 6% MeOH in DCM) to afford the product (37 mg, 49% yield).

$[M+H]^+$ = 536.3

5-N-[[3-(Imidazo[1,2-a]pyridin-8-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methyl]isoquinoline-1,5-diamine (Example 1018)



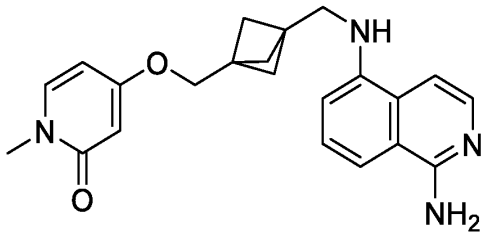
1-N-[(2,4-Dimethoxyphenyl)methyl]-5-N-[[3-(imidazo[1,2-a]pyridin-8-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methyl]isoquinoline-1,5-diamine (37 mg, 0.07 mmol) was deprotected according to General Method **8** at 50 °C for 60 min. Following SCX the crude product was purified by automated prep HPLC (mass directed 2-60% MeCN in water with a basic mobile phase of 0.1% NH_3 in water over 20 min) and lyophilised to afford the product (10 mg, 38% yield).

$[M+H]^+$ = 386.2

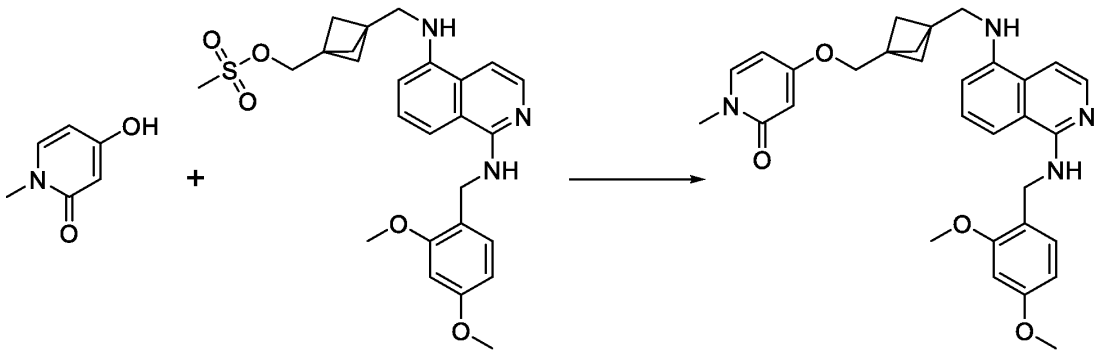
^{1}H NMR (DMSO-d_6, 400 MHz) δ 1.76 (6H, s), 4.17 (2H, s), 5.86 (1H, t, J = 5.9 Hz), 6.46 (2H, s), 6.58 (1H, d, J = 7.5 Hz), 6.65 (1H, d, J = 7.7 Hz), 6.72 (1H, t, J = 7.1 Hz), 7.14 (1H, d, J = 6.1 Hz), 7.19 (1H, t, J = 8.0 Hz), 7.30 (1H, d, J = 8.3 Hz), 7.44 (1H, s), 7.71 (1H, d, J = 6.0 Hz), 7.89 (1H, s), 8.11 (1H, d, J = 6.7 Hz). 2H masked by water peak (confirmed by COSY)

Example number 1019

4-[[3-[[(1-aminoisoquinolin-5-yl)amino]methyl]-1-bicyclo[1.1.1]pentanyl]methoxy]-1-methylpyridin-2-one



4-[[3-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-1-bicyclo[1.1.1]pentanyl]methoxy]-1-methylpyridin-2-one

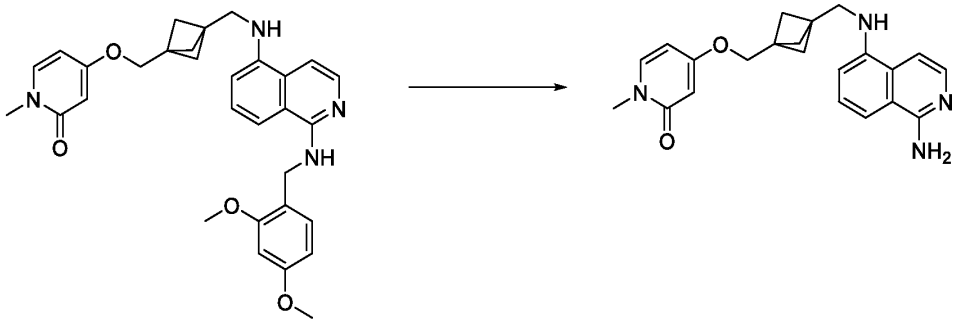


Following General Method **2b**, [3-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-1-bicyclo[1.1.1]pentanyl]methyl methanesulfonate (100 mg, 0.2 mmol) was reacted

with 4-hydroxy-1-methylpyridin-2-one (38 mg, 0.3 mmol) and K_2CO_3 (111 mg, 0.8 mmol) in MeCN (5 mL) in a sealed vial at 90 °C for 3 days. Purification by flash chromatography (Silica, 0 - 20% MeOH in DCM) afforded the product (52 mg, 44% yield).

$[M+H]^+$ = 527.3

4-[[3-[[(1-Aminoisoquinolin-5-yl)amino]methyl]-1-bicyclo[1.1.1]pentanyl]methoxy]-1-methylpyridin-2-one (Example 1019)



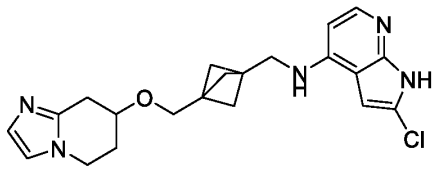
Deprotection of 4-[[3-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-1-bicyclo[1.1.1]pentanyl]methoxy]-1-methylpyridin-2-one (52 mg, 0.09 mmol) was carried out using General Method **8**. After SCX and purification by automated prep HPLC (mass directed 2-60% MeCN in water with a basic mobile phase of 0.1% NH_3 in water over 20 min), lyophilisation afforded the product (6 mg, 18% yield).

$[M+H]^+$ = 377.2

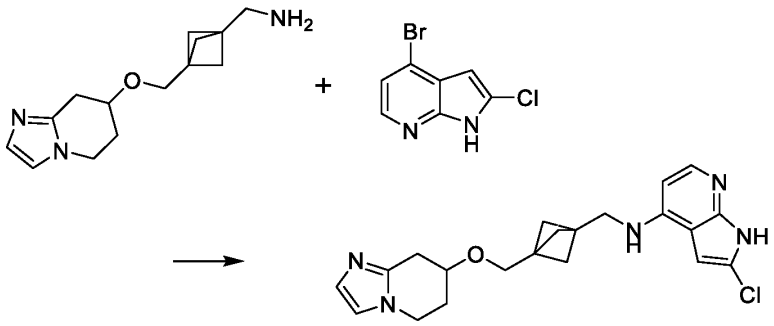
^1H NMR (DMSO-d6, 400 MHz) δ 1.71 (6H, s), 3.31 (3H,s), 3.95 (2H, s), 5.74 (1H, d, J = 2.7 Hz), 5.86 - 5.90 (2H, m), 6.48 (2H, s), 6.64 (1H, d, J = 7.7 Hz), 7.14 (1H, d, J = 6.2 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.31 (1H, d, J = 8.3 Hz), 7.53 (1H, d, J = 7.7 Hz), 7.71 (1H, d, J = 6.1 Hz). 2H masked by water peak.

Example number 1130

2-Chloro-N-[[3-(5,6,7,8-tetrahydroimidazo[1,2-a]pyridin-7-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methyl]-1H-pyrrolo[2,3-b]pyridin-4-amine



2-Chloro-N-[[3-(5,6,7,8-tetrahydroimidazo[1,2-a]pyridin-7-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methyl]-1H-pyrrolo[2,3-b]pyridin-4-amine (Example 1130)

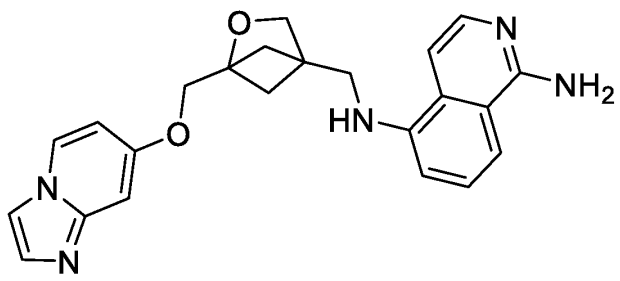


According to a modification of General Method **4**, to a screw-capped pressure vial was added [3-(5,6,7,8-tetrahydroimidazo[1,2-a]pyridin-7-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methanamine (130 mg, 0.53 mmol) and 4-bromo-2-chloro-1H-pyrrolo[2,3-b]pyridine (122 mg, 0.53 mmol). THF (2 mL) was added followed by LiHMDS (1M in THF) (2.63 mL, 2.63 mmol). The solution was purged with nitrogen for 5 min before tert-BuBrettphos Pd G3 (22 mg, 0.03 mmol) was added. The vial was sealed and the mixture was purged with nitrogen for a further 5 minutes before stirring at 70 °C for 5 days. 1,4-Dioxane (5 mL), LiHMDS (1M in THF) (2.63 mL, 2.63 mmol) and Brettphos Pd G3 (24 mg, 0.03 mmol) were added and the reaction mixture was purged with nitrogen for 10 minutes. The reaction mixture was stirred at 70 °C overnight. The reaction was quenched with AcOH (2.0 eq) and concentrated. The crude was purified by an SCX eluting with NH_3 in MeOH followed by purification by flash chromatography and prep HPLC. $[M+H]^+ = 398.2$

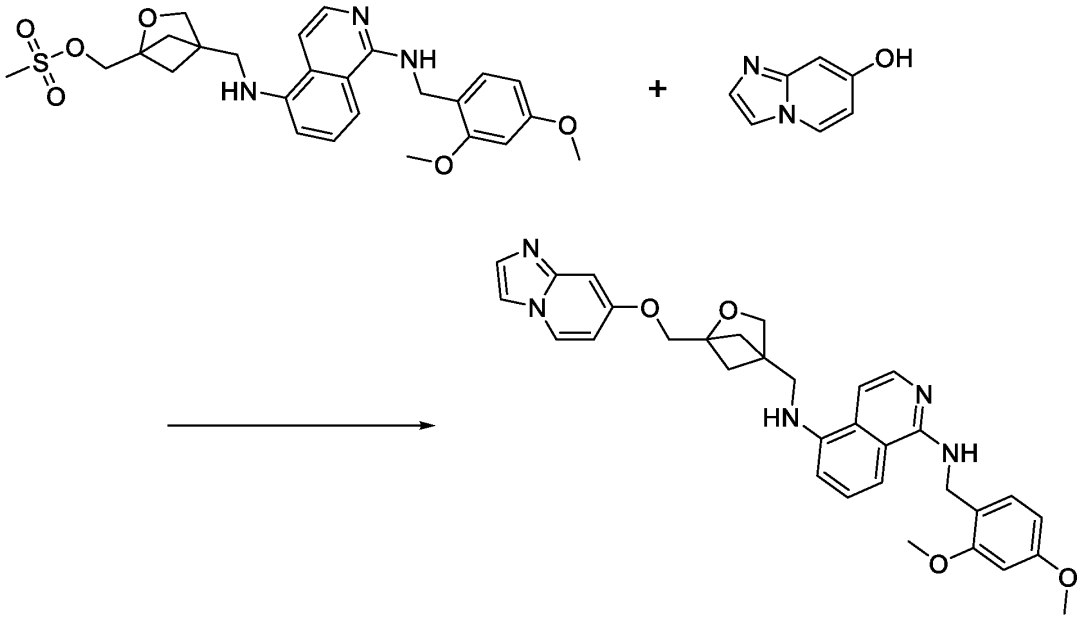
^{1}H NMR (DMSO, 400 MHz) δ 1.59 (6H, s), 1.95 - 2.05 (2H, m), 2.68 (1H, dd, J = 16.6, 5.6 Hz), 2.94 (1H, dd, J = 16.5, 4.6 Hz), 3.30 (2H, d, J = 6.0 Hz), 3.41 - 3.48 (2H, m), 3.90 (3H, td, J = 6.2, 2.5 Hz), 6.14 (1H, d, J = 5.8 Hz), 6.53 (1H, s), 6.57 (1H, s), 6.78 (1H, d, J = 1.2 Hz), 6.96 (1H, d, J = 1.2 Hz), 7.73 (1H, d, J = 5.6 Hz), 11.93 (1H, s)

Example number 2020

5-N-[[1-(Imidazo[1,2-a]pyridin-7-yloxymethyl)-2-oxabicyclo[2.1.1]hexan-4-yl]methyl]isoquinoline-1,5-diamine



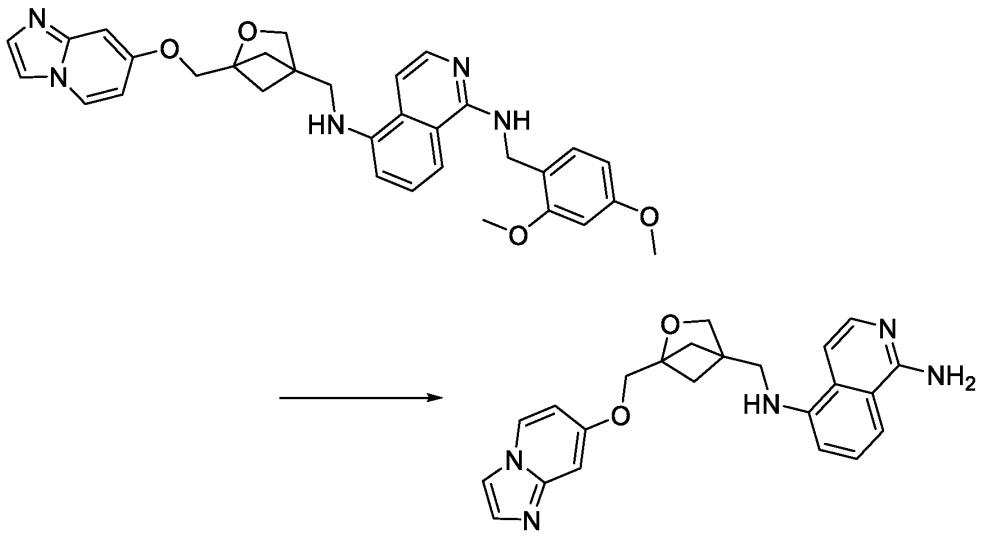
1-N-[(2,4-Dimethoxyphenyl)methyl]-5-N-[[1-(imidazo[1,2-a]pyridin-7-yloxymethyl)-2-oxabicyclo[2.1.1]hexan-4-yl]methyl]isoquinoline-1,5-diamine



According to General Method **2a**, to a solution of imidazo[1,2-a]pyridin-7-ol hydrochloride (100 mg, 0.59 mmol) and [4-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-2-oxabicyclo[2.1.1]hexan-1-yl]methyl methanesulfonate (250 mg, 0.49 mmol) in DMF (6 mL) was added NaH (60% in mineral oil) (70 mg, 1.75 mmol) in an ice/water bath. The mixture was stirred for 5 min, then allowed to warm to rt for 5 min. The mixture was heated at 50 °C for 2 days, quenched with water (10 mL) and concentrated, azeotroping with toluene. Flash chromatography (silica, 0-15% MeOH in EtOAc) afforded the product (173 mg, 64% yield).

$[M+H]^+$ = 552.3

5-N-[[1-(Imidazo[1,2-a]pyridin-7-yloxymethyl)-2-oxabicyclo[2.1.1]hexan-4-yl]methyl]isoquinoline-1,5-diamine (Example 2020)



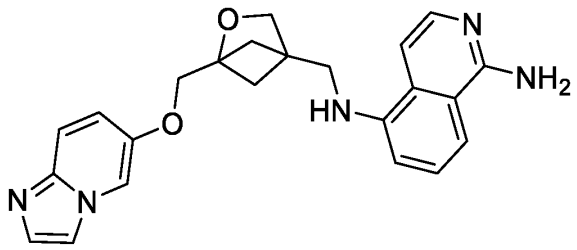
1-N-[(2,4-Dimethoxyphenyl)methyl]-5-N-[[1-(imidazo[1,2-a]pyridin-7-yloxymethyl)-2-oxabicyclo[2.1.1]hexan-4-yl]methyl]isoquinoline-1,5-diamine (137 mg , 0.25 mmol) was reacted according to General Method **8**. The product was purified by flash chromatography (silica, 50-100% EtOAc in Pet. Ether followed by 0-17% MeOH in EtOAc) and lyophilized to afford the product (57 mg, 57% yield).

LCMS: $[M+H]^+$ = 402.2

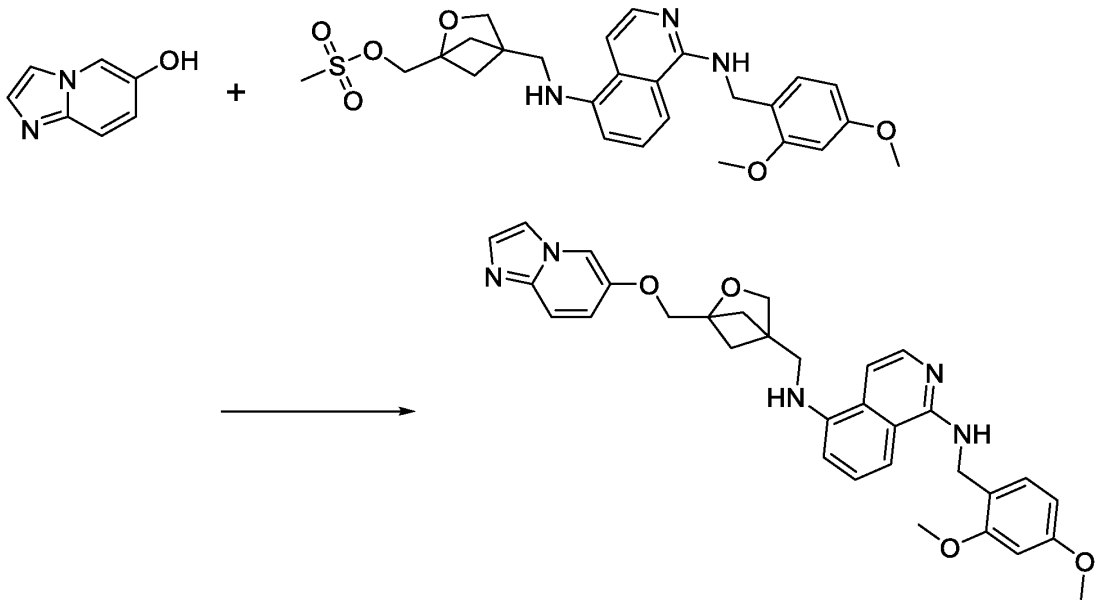
^{1}H NMR (DMSO-d6, 400 MHz) δ 1.61 (2H, dd, J = 4.4, 1.7 Hz), 1.85 (2H, dd, J = 4.4, 1.7 Hz), 3.58 (2H, d, J = 5.9 Hz), 3.71 (2H, s), 4.25 (2H, s), 5.99 (1H, t, J = 5.9 Hz), 6.48 (2H, s), 6.59 (1H, dd, J = 7.4, 2.5 Hz), 6.68 (1H, d, J = 7.7 Hz), 6.93 (1H, d, J = 2.5 Hz), 7.17 (1H, d, J = 6.1 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.32 (1H, d, J = 8.3 Hz), 7.37 (1H, d, J = 1.3 Hz), 7.68 - 7.76 (2H, m), 8.36 (1H, d, J = 7.4 Hz)

Example number 2022

5-N-[[1-(Imidazo[1,2-a]pyridin-6-yloxymethyl)-2-oxabicyclo[2.1.1]hexan-4-yl]methyl]isoquinoline-1,5-diamine



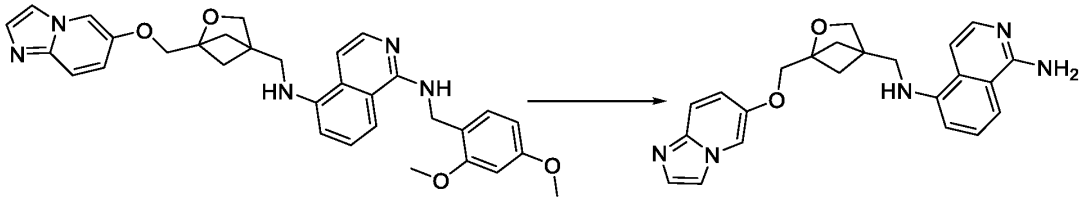
1-N-[(2,4-Dimethoxyphenyl)methyl]-5-N-[[1-(imidazo[1,2-a]pyridin-6-yloxymethyl)-2-oxabicyclo[2.1.1]hexan-4-yl]methyl]isoquinoline-1,5-diamine



According to General Method **2b,** [4-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-2-oxabicyclo[2.1.1]hexan-1-yl]methyl methanesulfonate (265 mg, 0.52 mmol) was reacted with imidazo[1,2-a]pyridin-6-ol (104 mg, 0.77 mmol) and K_2CO_3 (285 mg, 2.06 mmol) in MeCN (7 mL) at 90 °C for 3 days. The mixture was cooled to rt and filtered through filter paper, washing with EtOAc (50 mL) and MeOH (10 mL), and the filtrate was concentrated. The residue was purified by flash chromatography (silica, 0-100% EtOAc in Pet. Ether followed by 0-20% MeOH in EtOAc) to afford the product (186 mg, 65% yield).

$[M+H]^+$ = 552.3

5-N-[[1-(Imidazo[1,2-a]pyridin-6-yloxymethyl)-2-oxabicyclo[2.1.1]hexan-4-yl]methyl]isoquinoline-1,5-diamine (Example 2022)



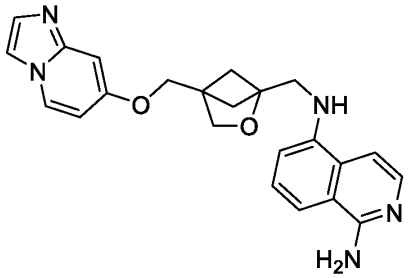
1-N-[(2,4-Dimethoxyphenyl)methyl]-5-N-[[1-(imidazo[1,2-a]pyridin-6-yloxymethyl)-2-oxabicyclo[2.1.1]hexan-4-yl]methyl]isoquinoline-1,5-diamine (186 mg, 0.34 mmol) was reacted according to General Method **8**. The crude product was purified by flash chromatography (silica, 0-100% EtOAc in Pet. Ether followed by 0-17% MeOH in EtOAc) and lyophilized to afford the product (50 mg, 37% yield).

$[M+H]^+ = 402.2$

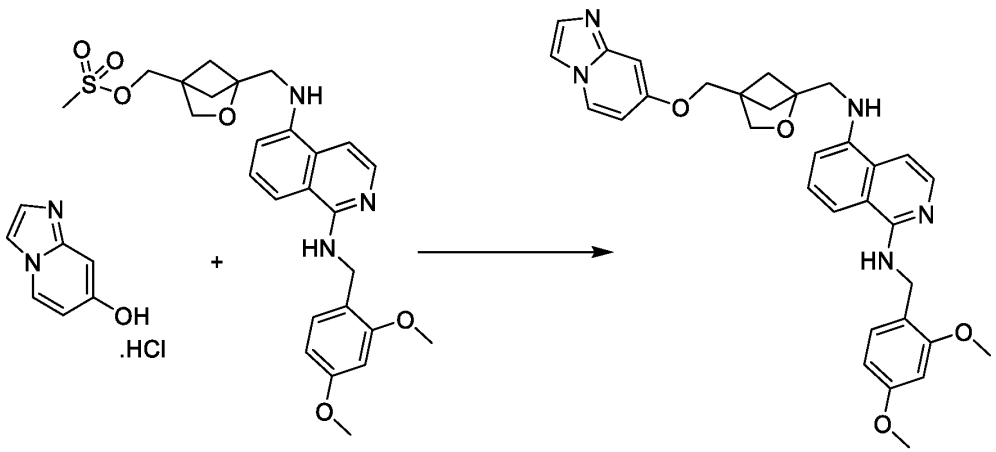
^1H NMR (DMSO-d6, 400 MHz) δ 1.62 (2H, dd, J = 4.5, 1.7 Hz), 1.85 (2H, dd, J = 4.4, 1.7 Hz), 3.59 (2H, d, J = 5.9 Hz), 3.71 (2H, s), 4.17 (2H, s), 6.00 (1H, t, J = 6.0 Hz), 6.48 (2H, s), 6.69 (1H, d, J = 7.7 Hz), 7.02 (1H, dd, J = 9.7, 2.4 Hz), 7.13 - 7.27 (2H, m), 7.33 (1H, d, J = 8.3 Hz), 7.42 - 7.51 (2H, m), 7.72 (1H, d, J = 6.1 Hz), 7.81 (1H, t, J = 0.9 Hz), 8.24 - 8.30 (1H, m)

Example number 6601

5-N-[[4-(Imidazo[1,2-a]pyridin-7-yloxymethyl)-2-oxabicyclo[2.1.1]hexan-1-yl]methyl]isoquinoline-1,5-diamine



1-N-[(2,4-Dimethoxyphenyl)methyl]-5-N-[[4-(imidazo[1,2-a]pyridin-7-yloxymethyl)-2-oxabicyclo[2.1.1]hexan-1-yl]methyl]isoquinoline-1,5-diamine

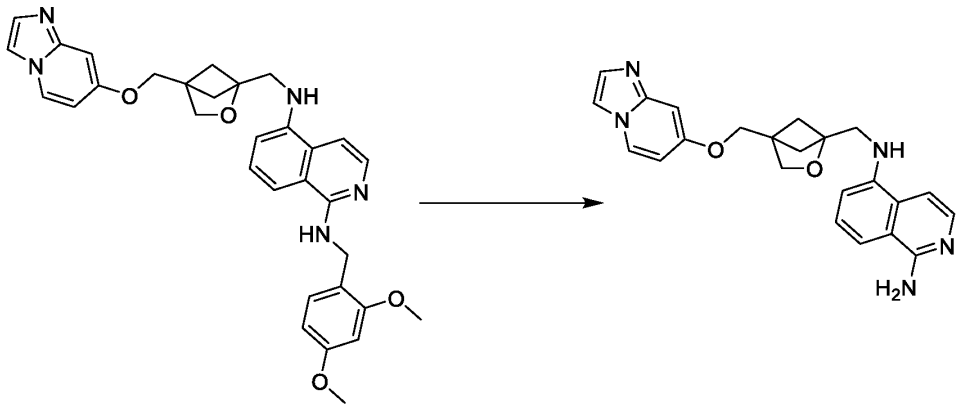


Following General Method **2a**, imidazo[1,2-a]pyridin-7-ol hydrochloride (80 mg, 0.47 mmol) was reacted with[1-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-2-oxabicyclo[2.1.1]hexan-4-yl]methyl methanesulfonate (200 mg, 0.39 mmol) in DMF (5 mL) with NaH (60% in mineral oil) (56 mg, 1.4 mmol) for 18 h. The reaction mixture was diluted with water (10 mL) and EtOAc (20 mL). The layers were separated, and the aqueous layers were back-extracted with EtOAc (3 x 10 mL).

The organic layers were combined, dried ($MgSO_4$) and concentrated, azeotroping with toluene. Flash chromatography (silica, 0-15% MeOH in EtOAc) afforded the product (125 mg, 58% yield).

LCMS: $[M+H]^+$ = 552.3

5-N-[[4-(Imidazo[1,2-a]pyridin-7-yloxymethyl)-2-oxabicyclo[2.1.1]hexan-1-yl]methyl]isoquinoline-1,5-diamine (Example 6601)



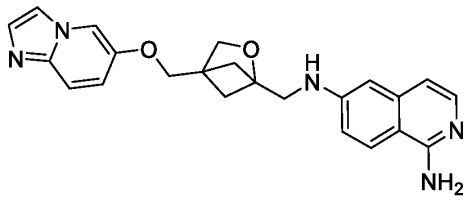
1-N-[(2,4-Dimethoxyphenyl)methyl]-5-N-[[4-(imidazo[1,2-a]pyridin-7-yloxymethyl)-2-oxabicyclo[2.1.1]hexan-1-yl]methyl]isoquinoline-1,5-diamine (125 mg, 0.23 mmol) was deprotected according to General Method **8**, in TFA (2 mL, 26.12 mmol) at rt for 60 min. The reaction mixture was concentrated *in vacuo* before being passed directly through an SCX and washing with MeOH. The product was eluted with a solution of 7M NH_3 in MeOH and concentrated. The residue was purified by automated prep HPLC (mass directed 2-60% over 20 min in basic mobile phase) and lyophilised to afford to afford the product (52 mg, 57% yield) as a solid.

LCMS: $[M+H]^+$ = 402.2

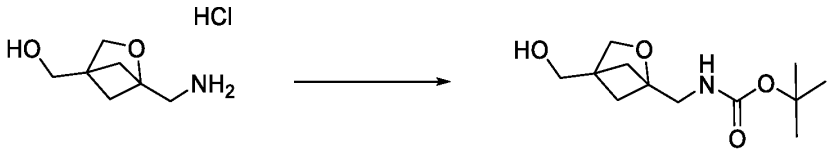
^1H NMR ($CDCl_3$, 400 MHz) δ 1.82 - 1.97 (4H, m), 3.63 (2H, d, J = 5.2 Hz), 3.91 (2H, s), 4.28 (2H, s), 4.66 (1H, s), 5.10 (2H, s), 6.52 (1H, dd, J = 7.4, 2.4 Hz), 6.75 (1H, d, J = 7.7 Hz), 6.86 (1H, d, J = 2.4 Hz), 7.00 (1H, d, J = 6.1 Hz), 7.15 (1H, d, J = 8.3 Hz), 7.36 (1H, t, J = 8.0 Hz), 7.42 (1H, s), 7.49 (1H, d, J = 1.4 Hz), 7.94 (2H, dd, J = 6.8, 5.5 Hz) ppm.

Example number 6602

5-N-[[4-(Imidazo[1,2-a]pyridin-6-yloxymethyl)-2-oxabicyclo[2.1.1]hexan-1-yl]methyl]isoquinoline-1,5-diamine



tert-Butyl N-[[4-(hydroxymethyl)-2-oxabicyclo[2.1.1]hexan-1-yl]methyl]carbamate

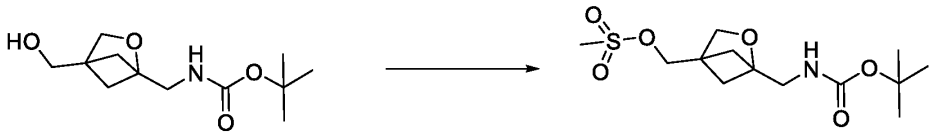


To a solution of [1-(aminomethyl)-2-oxabicyclo[2.1.1]hexan-4-yl]methanol hydrochloride (1000 mg, 5.57 mmol) and TEA (2716 µL, 19.5 mmol) in THF (30 mL) at 0 °C was added Boc_2O (1460 mg, 6.68 mmol) and the mixture was stirred for 10 min at 0 °C. After that time the reaction was stirred for 18 h at rt. The reaction was quenched with water (30 mL) and washed with EtOAc (2 x 50 mL), dried ($MgSO_4$) and concentrated. The crude product was purified by flash chromatography (Silica, 0-20% MeOH in DCM) to afford the product (1010 mg, 75% yield).

$[M+Na]^+$ = 266.0

^1H NMR ($CDCl_3$, 400 MHz) δ 1.45 (9H, s), 1.58 (2H, dd, J = 4.6, 1.7 Hz), 1.68 (2H, dd, J = 4.6, 1.7 Hz), 1.98 - 2.08 (1H, m), 3.46 (2H, d, J = 6.0 Hz), 3.70 (2H, s), 3.89 (2H, d, J = 4.7 Hz), 4.92 (1H, s)

[1-[[2-Methylpropan-2-yl)oxycarbonylamino]methyl]-2-oxabicyclo[2.1.1]hexan-1-yl]methyl]methanesulfonate

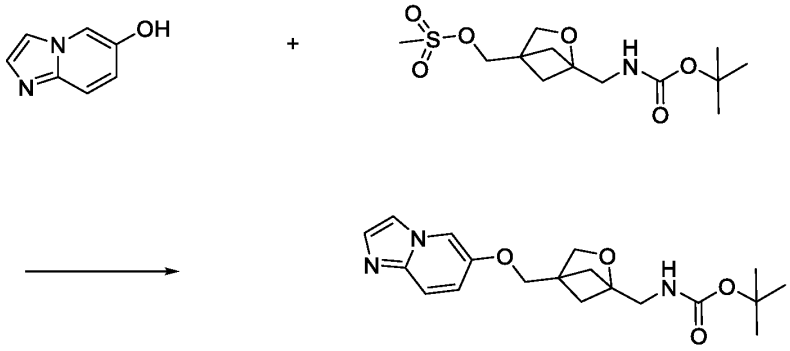


According to a modification of General method **1a**, a solution of tert-butyl N-[[4-(hydroxymethyl)-2-oxabicyclo[2.1.1]hexan-1-yl]methyl]carbamate (1010 mg, 4.16 mmol) in DCM (30 mL) was cooled in an ice bath. MsCl (100 µL, 1.29 mmol) and TEA (547 mg, 5.4 mmol) were added dropwise sequentially whilst maintaining the temperature at 0 °C. The mixture was stirred at rt for 90 min, after which time it was quenched with water (10 mL) and washed with DCM (2 x 25 mL). The combined organic layers were washed with water (3 x 25 mL), brine (20 mL), dried ($MgSO_4$) and concentrated. The productl crystalised on standing and was triturated with Et_2O (10 mL) to afford the product (1010 mg, 76% yield)

$[M+Na]^+$ = 344.2

^1H NMR ($CDCl_3$, 400 MHz) δ 1.44 (9H, s), 1.67 (2H, dd, J = 4.7, 1.7 Hz), 1.76 (2H, dd, J = 4.7, 1.7 Hz), 3.04 (3H, s), 3.47 (2H, d, J = 5.9 Hz), 3.73 (2H, s), 4.48 (2H, s), 4.84 (1H, s)

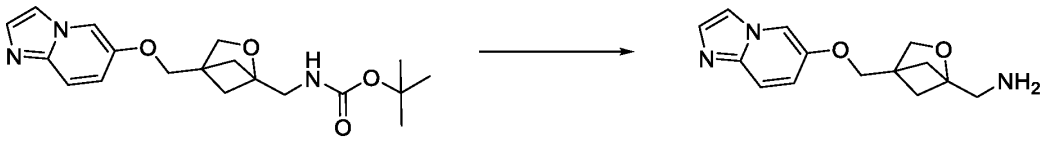
N-[[4-(Imidazo[1,2-a]pyridin-6-yloxymethyl)-2-oxabicyclo[2.1.1]hexan-1-yl]methyl]carbamate



According to a modification of General Method **2a**, [1-[[(2-methylpropan-2-yl)oxycarbonylamino]methyl]-2-oxabicyclo[2.1.1]hexan-4-yl]methyl methanesulfonate (100 mg, 0.31 mmol) and imidazo[1,2-a]pyridin-6-ol (83.0 mg, 0.62 mmol) were dissolved in DMF (3 mL). NaH, 60%w/w in mineral oil (37.0 mg, 0.93 mmol) and 4Å molecular sieves were added and the reaction stirred at 50 °C for 18 h. The reaction was cooled to rt, quenched with brine (10 mL), filtered through Celite® and concentrated. The crude product was purified by flash chromatography (Silica, 0-25% MeOH in EtOAc) to afford the product (84.0 mg, 75% yield).

$[M+H]^+$ = 360.2

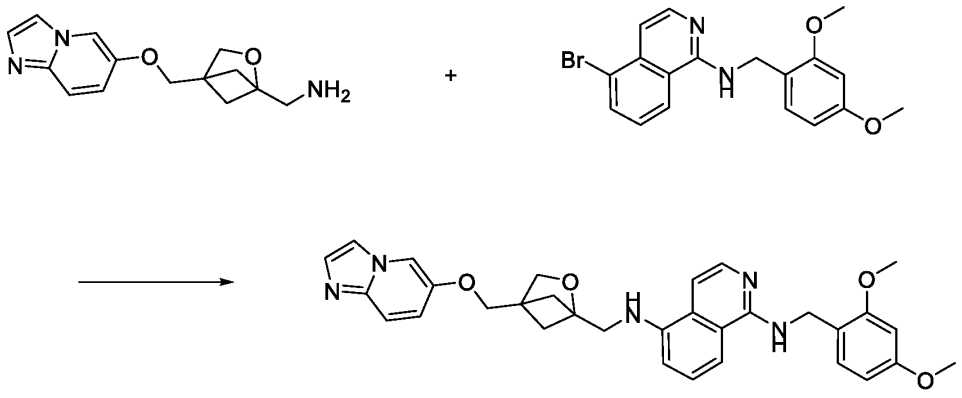
[4-(Imidazo[1,2-a]pyridin-6-yloxymethyl)-2-oxabicyclo[2.1.1]hexan-1-yl]methanamine



According to a modification of General Method **5a**, to a solution of tert-butyl N-[[4-(imidazo[1,2-a]pyridin-6-yloxymethyl)-2-oxabicyclo[2.1.1]hexan-1-yl]methyl]carbamate (84.0 mg, 0.23 mmol) in DCM (5 mL) was added 4M HCl in dioxane (950 µL, 3.8 mmol). The reaction was stirred at rt for 3 h and then concentrated and freebased using bicarbonate resin to afford the product (60.0 mg, 99% yield).

$[M+H]^+$ = 260.2

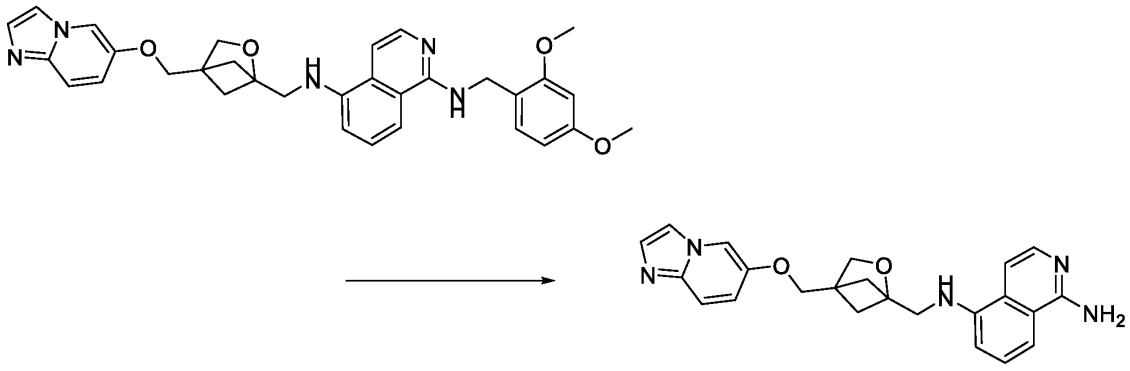
1-N-[(2,4-Dimethoxyphenyl)methyl]-5-N-[[4-(imidazo[1,2-a]pyridin-6-yloxymethyl)-2-oxabicyclo[2.1.1]hexan-1-yl]methyl]isoquinoline-1,5-diamine



According to a modification of General Method **4**, [4-(imidazo[1,2-a]pyridin-6-yloxymethyl)-2-oxabicyclo[2.1.1]hexan-1-yl]methanamine (60 mg, 0.23 mmol) was reacted with 5-bromo-N-(2,4-dimethoxybenzyl)isoquinolin-1-amine (130 mg, 0.35 mmol) in 1,4-dioxane (2 mL) in the presence of Brettphos Pd G4 (21 mg, 0.02 mmol) and NaO^{t}Bu (67.0 mg, 0.69 mmol) at 60 °C for 24 h. The crude residue was purified by flash chromatography (Silica, 0 - 20% MeOH in EtOAc) to afford the product (101 mg, , 79% yield).

$[M+H]^+$ = 552.3

5-N-[[4-(Imidazo[1,2-a]pyridin-6-yloxymethyl)-2-oxabicyclo[2.1.1]hexan-1-yl]methyl]isoquinoline-1,5-diamine (Example 6602)



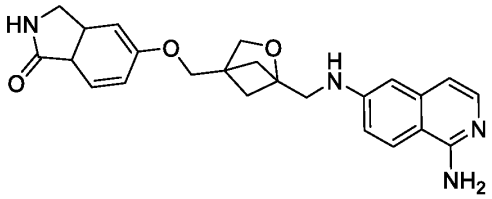
According to General method **8**, 1-N-[(2,4-dimethoxyphenyl)methyl]-5-N-[[4-(imidazo[1,2-a]pyridin-6-yloxymethyl)-2-oxabicyclo[2.1.1]hexan-1-yl]methyl]isoquinoline-1,5-diamine (101 mg, 0.18 mmol) was deprotected. After SCX the crude was purified by automated prep HPLC (mass directed 2-60% over 20 min in a basic mobile phase) and lyophilised to afford the product (34.0 mg, 47% yield).

$[M+H]^+$ = 402.2

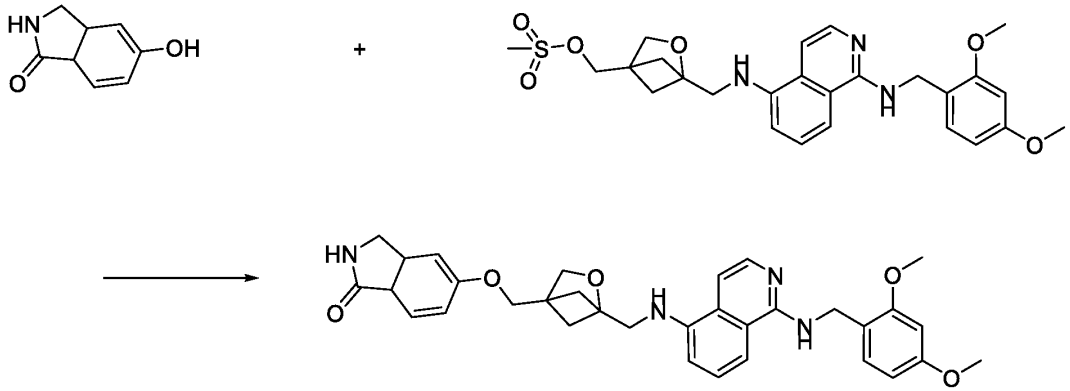
^{1}H NMR (DMSO-d6, 400 MHz) δ 1.60 (2H, dd, J = 4.5, 1.7 Hz), 1.86 (2H, dd, J = 4.5, 1.7 Hz), 3.55 (2H, d, J = 5.9 Hz), 3.74 (2H, s), 4.24 (2H, s), 5.92 (1H, t, J = 6.0 Hz), 6.50 (2H, s), 6.70 (1H, d, J = 7.7 Hz), 7.01 (1H, dd, J = 9.7, 2.4 Hz), 7.11 (1H, d, J = 6.1 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.34 (1H, d, J = 8.3 Hz), 7.45 (1H, d, J = 9.8 Hz), 7.49 (1H, d, J = 1.1 Hz), 7.72 (1H, d, J = 6.1 Hz), 7.80 (1H, t, J = 0.9 Hz), 8.28 (1H, dd, J = 2.5, 0.8 Hz)

Example number 6618

5-[[1-[[(1-Aminoisoquinolin-5-yl)amino]methyl]-2-oxabicyclo[2.1.1]hexan-4-yl]methoxy]-2,3-dihydroisoindol-1-one

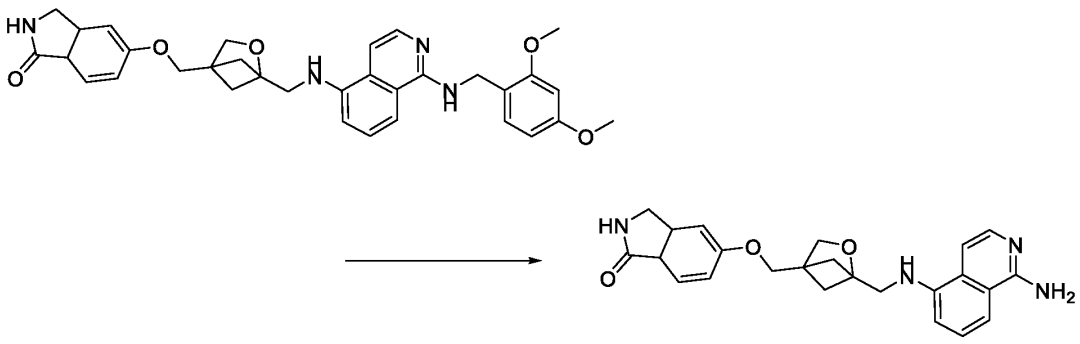


5-[[1-[[[1-[(2,4-Dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-2-oxabicyclo[2.1.1]hexan-4-yl]methoxy]-2,3-dihydroisoindol-1-one



According to a modification of General Method **2a**, [1-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-2-oxabicyclo[2.1.1]hexan-4-yl]methyl methanesulfonate (400 mg, 0.78 mmol) was reacted with 5-hydroxyisoindolin-1-one (128 mg, 0.86 mmol) at 50 °C for 18 h. The reaction mixture was quenched with 1:1 brine/water (15 mL) and extracted with EtOAc (3 x 20 mL). Organic layers were combined, dried ($MgSO_4$) and concentrated. Residual DMF was removed by azeotroping with toluene. The crude material was purified via flash chromatography (Silica, 0-100% (2% NH_4OH in 3:3:1 EtOAc/MeCN/EtOH) in Pet. Ether) to afford the product (189 mg, 43% yield). $[M+H]^+$ = 567.5

5-[[1-[[(1-Aminoisoquinolin-5-yl)amino]methyl]-2-oxabicyclo[2.1.1]hexan-4-yl]methoxy]-2,3-dihydroisoindol-1-one (Example 6618)

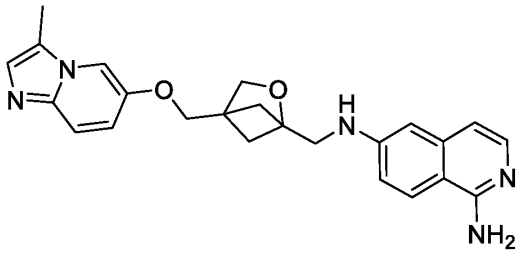


According to a modification of General method **8**, 5-[[1-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-2-oxabicyclo[2.1.1]hexan-4-yl]methoxy]-2,3-dihydroisoindol-1-one (189 mg, 0.33 mmol) was deprotected at rt for 2 h. After SCX, the crude was purified via prep-HPLC (mass directed 2-60% in basic mobile phase) then further purified via prep-HPLC (2-60% in acidic mobile phase). The material was lyophilised to afford the product (30 mg, 19% yield). $[M+H]^+ = 417.4$

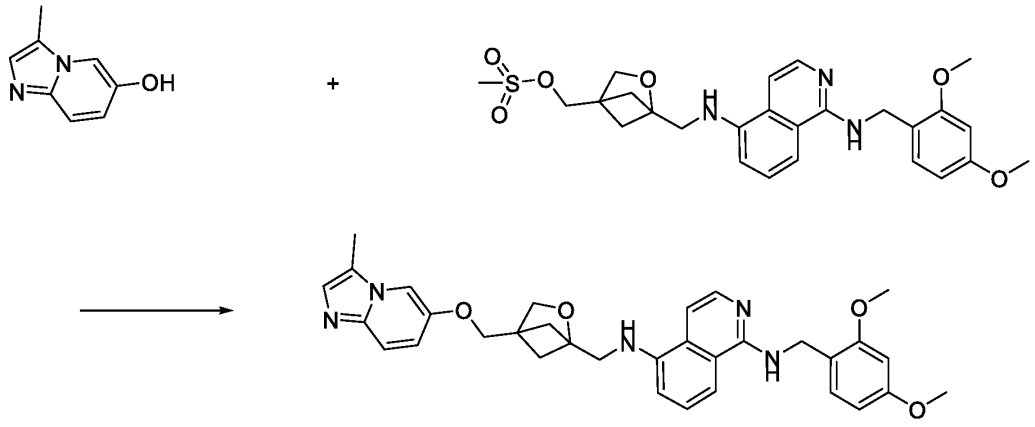
^{1}H NMR (DMSO, 400 MHz) δ 1.58 (2H, dd, J = 4.5, 1.7 Hz), 1.84 (2H, dd, J = 4.6, 1.7 Hz), 3.54 (2H, d, J = 5.6 Hz), 3.72 (2H, s), 4.28 (2H, s), 4.33 (2H, s), 5.94 (1H, t, J = 6.0 Hz), 6.59 (2H, s), 6.70 (1H, d, J = 7.7 Hz), 7.01 (1H, dd, J = 8.4, 2.3 Hz), 7.08 - 7.16 (2H, m), 7.21 (1H, t, J = 8.0 Hz), 7.34 (1H, d, J = 8.3 Hz), 7.53 (1H, d, J = 8.4 Hz), 7.71 (1H, d, J = 6.1 Hz), 8.27 (1H, s), 8.31 (1H, s)

Example number 6624

5-N-[[4-[(3-Methylimidazo[1,2-a]pyridin-6-yl)oxymethyl]-2-oxabicyclo[2.1.1]hexan-1-yl]methyl]isoquinoline-1,5-diamine



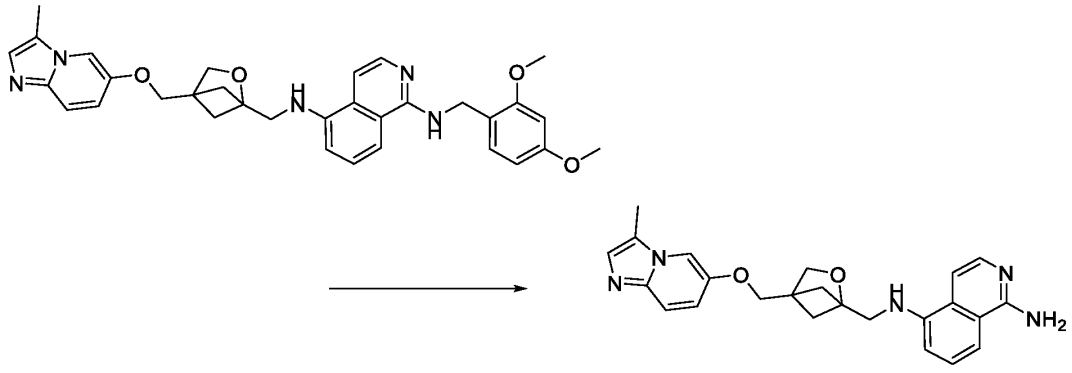
1-N-[(2,4-Dimethoxyphenyl)methyl]-5-N-[[4-[(3-methylimidazo[1,2-a]pyridin-6-yl)oxymethyl]-2-oxabicyclo[2.1.1]hexan-1-yl]methyl]isoquinoline-1,5-diamine



According to a modification of General Method **2a**, 3-methylimidazo[1,2-a]pyridin-6-ol (75 mg, 0.38 mmol) was reacted with [1-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-2-oxabicyclo[2.1.1]hexan-4-yl]methyl methanesulfonate (195 mg, 0.38 mmol) at 50 °C for 18 h. The reaction mixture was diluted with EtOAc (10 mL) and quenched with brine (10 mL). The layers were separated and the aq layer was back extracted with EtOAc (2 x 15 mL). The organic layers were combined, dried ($MgSO_4$) and concentrated. The residue was purified via flash chromatography (Silica, 0-100% (2% NH_4OH in 3:3:1 EtOAc/MeCN/EtOH+) in Pet. Ether) to afford the product (120 mg, 39% yield).

$[M+H]^+ = 566.6$

5-N-[[4-[(3-Methylimidazo[1,2-a]pyridin-6-yl)oxymethyl]-2-oxabicyclo[2.1.1]hexan-1-yl]methyl]isoquinoline-1,5-diamine (Example 6624)



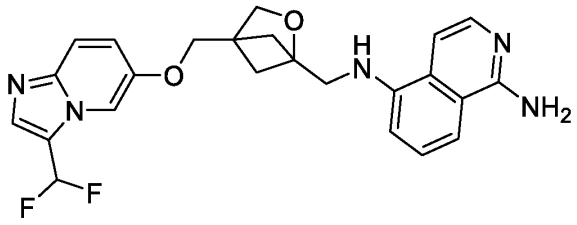
According to a modification of General Method **8**, a solution of 1-N-[(2,4-dimethoxyphenyl)methyl]-5-N-[[4-[(3-methylimidazo[1,2-a]pyridin-6-yl)oxymethyl]-2-oxabicyclo[2.1.1]hexan-1-yl]methyl]isoquinoline-1,5-diamine (120 mg, 0.15 mmol) in DCM (1 mL) was treated with TFA (2.10 mL, 27.26 mmol) and stirred at rt for 2 h and the reaction mixture was concentrated. After SCX work up the crude was purified via

automated prep HPLC (mass directed 2-60% over 20 mins in acidic mobile phase) and lyophilized to afford the product (41 mg, 54% yield). (Example 6624). $[M+H]^+$ = 416.4

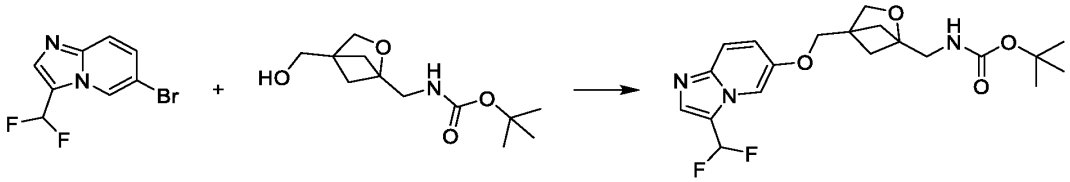
^{1}H (DMSO-d_6, 400 MHz) δ 1.61 (2H, dd, J = 4.2, 1.2 Hz), 1.87 (2H, d, J = 4.9 Hz), 2.41 (3H, s), 3.56 (2H, d, J = 5.4 Hz), 3.75 (2H, s), 4.32 (2H, s), 5.95 (1H, t, J = 5.8 Hz), 6.58 (2H, s), 6.71 (1H, d, J = 7.3 Hz), 6.99 (1H, dd, J = 9.7, 2.3 Hz), 7.11 (1H, d, J = 6.2 Hz), 7.22 (1H, t, J = 8.0 Hz), 7.29 (1H, s), 7.34 (1H, d, J = 8.3 Hz), 7.42 (1H, d, J = 9.7 Hz), 7.72 (1H, d, J = 6.1 Hz), 7.83 (1H, d, J = 2.1 Hz), 8.17 (2H, s)

Example Number 6644

5-N-[[4-[[3-(Difluoromethyl)imidazo[1,2-a]pyridin-6-yl]oxymethyl]-2-oxabicyclo[2.1.1]hexan-1-yl]methyl]isoquinoline-1,5-diamine



tert-ButylN-[[4-[[3-(difluoromethyl)imidazo[1,2-a]pyridin-6-yl]oxymethyl]-2-oxabicyclo[2.1.1]hexan-1-yl]methyl]carbamate

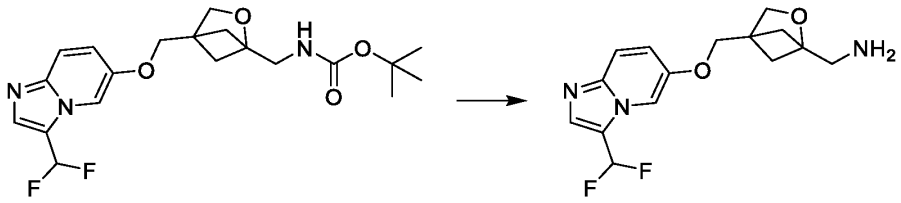


According to a modification of General Method **4**, tert-Butyl N-[[4-(hydroxymethyl)-2-oxabicyclo[2.1.1]hexan-1-yl]methyl]carbamate (250 mg, 1.03 mmol) and 6-bromo-3-(difluoromethyl)imidazo[1,2-a]pyridine (254 mg, 1.03 mmol) were dissolved in 1,4-dioxane (1028 µL). The solution was degassed with N_2(g) for 5 min before $CsCO_3$ (502 mg, 1.54 mmol) and RockPhos Pd G3 (17 mg, 0.02 mmol) were added then degassed with N_2(g) for 5 min. The mixture was sonicated and vortexed until the solids had dissolved or were finely suspended. The mixture was heated at 100 °C for 60 min. The mixture was cooled, retreated with RockPhos Pd G3 (17 mg, 0.02 mmol), degassed with N_2(g) and stirred at 100 °C for 1 h. The reaction was cooled, retreated with RockPhos Pd G3 (17 mg, 0.02 mmol), degassed with nitrogen and stirred at 100 °C for 1 h. The reaction was cooled, retreated with RockPhos Pd G3 (17

mg, 0.02 mmol), degassed with nitrogen and stirred at 100 °C for 18 h. The reaction was cooled, diluted with EtOAc (10 mL), filtered through celite and concentrated. The product was purified by flash chromatography (Silica, 0-100% EtOAc in Pet. Ether followed by 0 - 20% MeOH in EtOAc) to afford the product, (239 mg, 57% yield) as a solid.

$[M+H]^+$ = 410.2

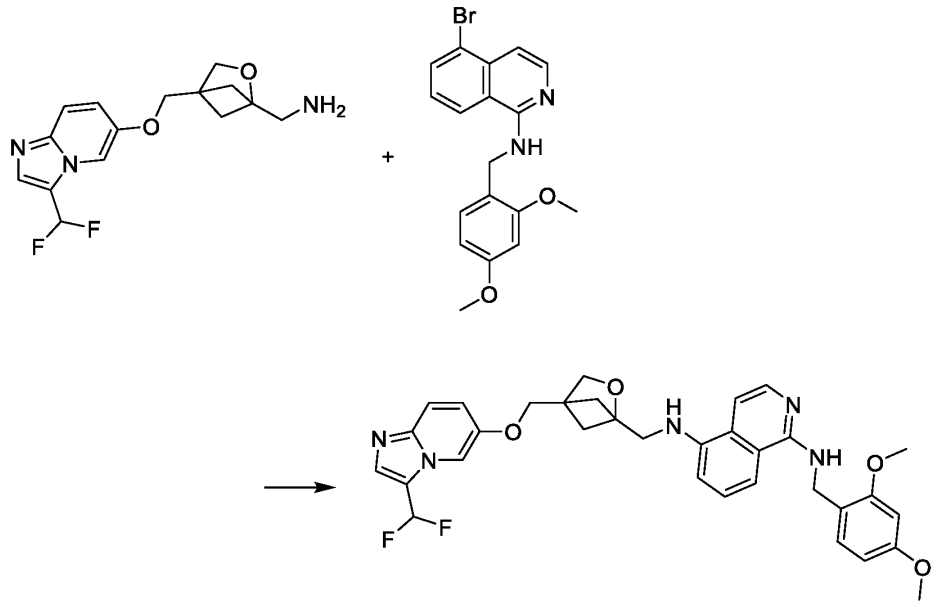
[4-[[3-(Difluoromethyl)imidazo[1,2-a]pyridin-6-yl]oxymethyl]-2-oxabicyclo[2.1.1]hexan-1-yl]methanamine



According to a modification of General Method **5a**, to a solution of tert-butyl N-[[4-[[3-(difluoromethyl)imidazo[1,2-a]pyridin-6-yl]oxymethyl]-2-oxabicyclo[2.1.1]hexan-1-yl]methyl]carbamate (230 mg, 0.56 mmol) in DCM (1 mL) was added 4M HCl in dioxane (702 µL, 2.81 mmol). The reaction was stirred at rt for 18 h and concentrated. The HCl salt was dissolved in methanol (5 mL), passed through bicarbonate resin cartridge twice and concentrated to afford the product, (155 mg, 89% yield) as an oil

$[M+H]^+$ = 310.1

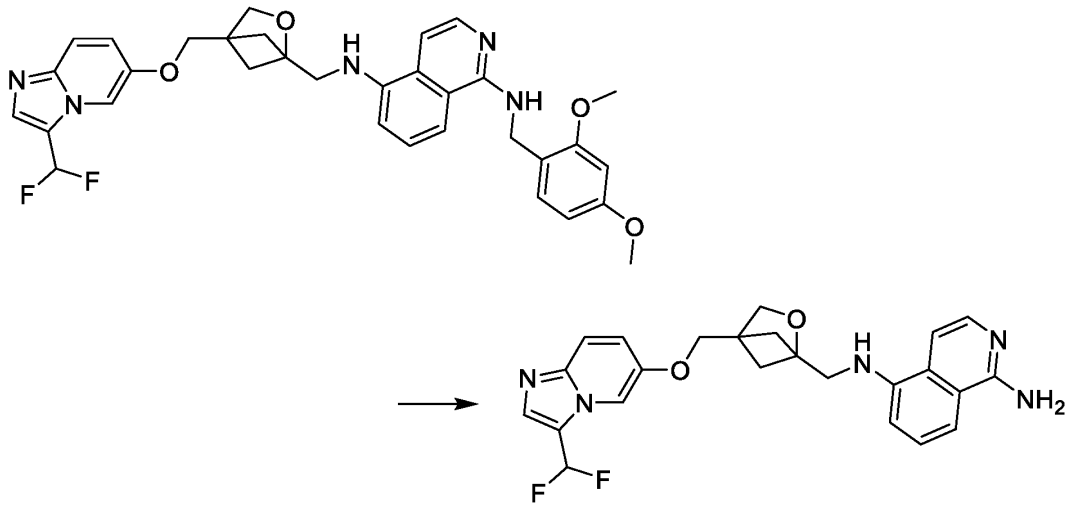
5-N-[[4-[[3-(Difluoromethyl)imidazo[1,2-a]pyridin-6-yl]oxymethyl]-2-oxabicyclo[2.1.1]hexan-1-yl]methyl]-1-N-[(2,4-dimethoxyphenyl)methyl]isoquinoline-1,5-diamine



To a screw capped pressure vial equipped with a stirrer bar was added tris(dibenzylideneacetone)dipalladium(0) (23 mg, 0.03 mmol), [4-[[3-(difluoromethyl)imidazo[1,2-a]pyridin-6-yl]oxymethyl]-2-oxabicyclo[2.1.1]hexan-1-yl]methanamine (155 mg, 0.5 mmol), [1-(2-diphenylphosphanylnaphthalen-1-yl)naphthalen-2-yl]-diphenylphosphane (8 mg, 0.01 mmol), 5-bromo-N-[(2,4-dimethoxyphenyl)methyl]isoquinolin-1-amine (206 mg, 0.55 mmol) and NaO^tBu (118 mg, 1.05 mmol). The vial was sealed and flushed with N_2(g) before 1,4-dioxane (5 mL) was added. The mixture was purged with N_2(g) for 5 min then stirred at 100 ˚C for 18 h. The mixture was cooled to rt, diluted with EtOAc (10 mL), filtered through a Celite, washed with EtOAc (3 x 10 mL) and concentrated. Flash chromatography (Silica, 0-100% EtOAc in Pet. Ether, followed by 0-20% MeOH in EtOAc) afforded the product, (193 mg, 64% yield).

$[M+H]^+$ = 602.3

5-N-[[4-[[3-(Difluoromethyl)imidazo[1,2-a]pyridin-6-yl]oxymethyl]-2-oxabicyclo[2.1.1]hexan-1-yl]methyl]isoquinoline-1,5-diamine (Example 6644)



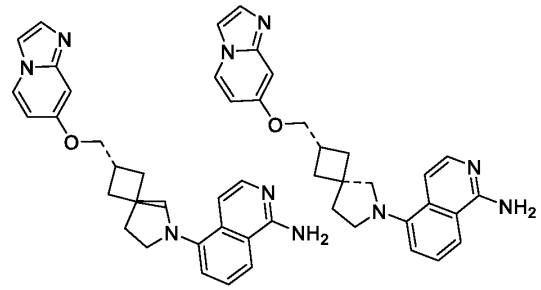
According to a modification of General Method **8**, a solution of 5-N-[[4-[[3-(difluoromethyl)imidazo[1,2-a]pyridin-6-yl]oxymethyl]-2-oxabicyclo[2.1.1]hexan-1-yl]methyl]-1-N-[(2,4-dimethoxyphenyl)methyl]isoquinoline-1,5-diamine (193 mg, 0.32 mmol) in TFA (1220 µL, 16.0 mmol) was stirred at rt for 60 min. The solvent was removed and the resulting solid was dissolved in meOH (3 mL), filtered and passed through SCX-2 and washed with MeOH (10 mL). The product was eluted with a solution of 1M NH_3 in MeOH (10 mL) and concentrated. Flash chromatography (Silica, 0-100% EtOAc in MeCN, then 0-20% MeOH in EtOAc) afforded the product (119 mg, 82% yield).

$[M+H]^+$ = 452.2

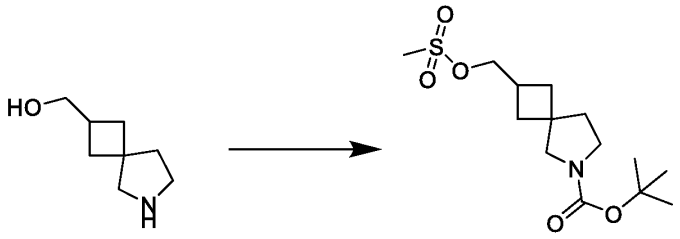
^{1}H NMR (DMSO-d6, 400 MHz) δ 1.61 (2H, dd, J = 4.5, 1.7 Hz), 1.87 (2H, dd, J = 4.5, 1.7 Hz), 3.56 (2H, d, J = 5.9 Hz), 3.75 (2H, s), 4.32 (2H, s), 5.93 (1H, t, J = 6.0 Hz), 6.50 (2H, s), 6.70 (1H, d, J = 7.7 Hz), 7.11 (1H, d, J = 6.1 Hz), 7.18 - 7.28 (2H, m), 7.34 (1H, d, J = 8.3 Hz), 7.44 (1H, t, J = 53.3 Hz), 7.61 - 7.64 (1H, m), 7.72 (1H, d, J = 6.1 Hz), 7.85 (1H, t, J = 2.0 Hz), 8.07 (1H, dd, J = 2.4, 0.8 Hz).

Example numbers 8806 and 8807

Trans* and cis* 5-(2-((imidazo[1,2-a]pyridin-7-yloxy)methyl)-6-azaspiro[3.4]octan-6-yl)isoquinolin-1-amine.



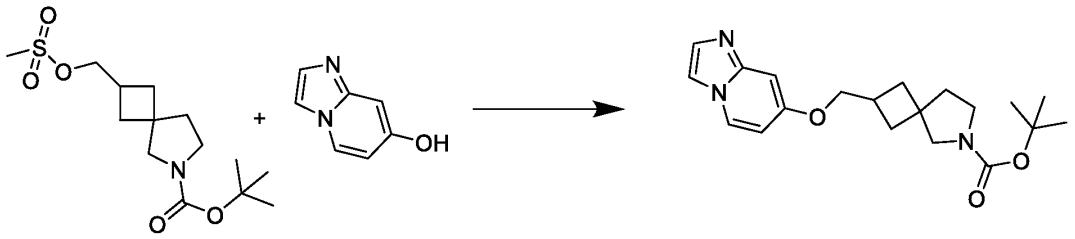
tert-Butyl 2-(methylsulfonyloxymethyl)-6-azaspiro[3.4]octane-6-carboxylate



According to a modification of General Method **1a**, to a solution of 6-azaspiro[3.4]octane-2-methanol (200 mg, 1.42 mmol) and TEA (987 µL, 7.08 mmol) in DCM (12 mL) at 0 °C was added Boc_2O (371 mg, 1.7 mmol) and the mixture was stirred for 1 h at 0 °C. After that time MsCl (164 µL, 2.12 mmol) was added at 0 °C and the reaction stirred for 30 min. The reaction was quenched with water (50 mL), washed with DCM (2 x 70 mL), dried ($MgSO_4$) and concentrated. The material was triturated with Et_2O to afford the product (452 mg, 100% yield) as a solid.

$[M+Na]^+ = 342.1$

tert-Butyl 2-((imidazo[1,2-a]pyridin-7-yloxy)methyl)-6-azaspiro[3.4]octane-6-carboxylate

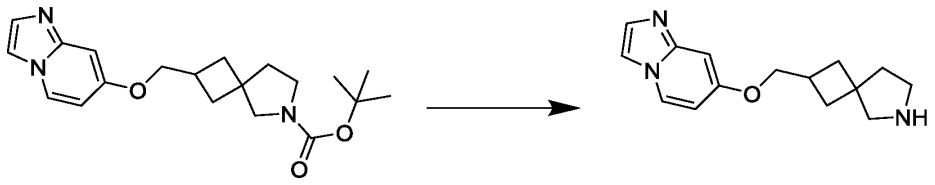


According to General Method **2b**, tert-butyl 2-(((methylsulfonyl)oxy)methyl)-6-azaspiro[3.4]octane-6-carboxylate (250 mg, 783 µmol) was reacted with imidazo[1,2-a]pyridin-7-ol (157 mg, 1.17 mmol) and K_2CO_3 (324 mg, 2.35 mmol) in DMF (10 mL) at 60 °C for 18 h. The crude was purified by chromatography (C18, 0-95% MeCN/10 mM NH_4HCO_3) to afford the product (100 mg, 34%) as an oil.

$[M+H]^+ = 358.2$

^1H NMR (CDCl3, 500 MHz) δ 1.44 (9H, d, J = 3.4 Hz), 1.74 - 2.00 (4H, m), 2.00 - 2.19 (2H, m), 2.74 (1H, p, J = 7.4 Hz),3.20 - 3.40 (4H, m), 3.93 (2H, d, J = 6.1 Hz), 6.49 (1H, dt, J = 7.4, 2.6 Hz), 6.83 (1H, d, J = 2.7 Hz), 7.39 (1H, s), 7.45 (1H,s), 7.92 (1H, d, J = 7.3 Hz)

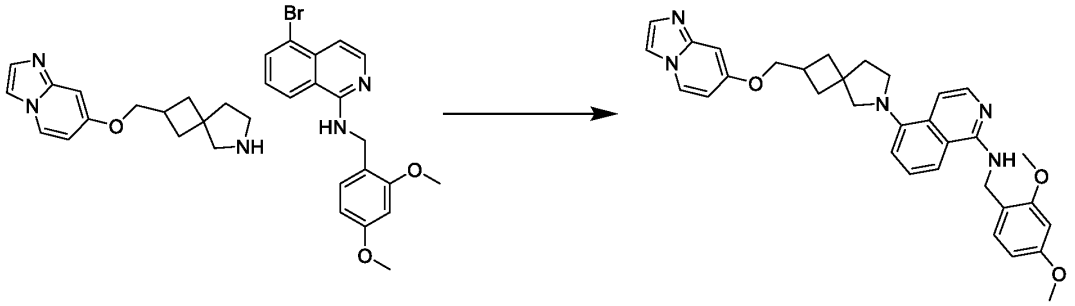
7-((6-Azaspiro[3.4]octan-2-yl)methoxy)imidazo[1,2-a]pyridine



According to a modification of General Method **5b**, tert-butyl 2-((imidazo[1,2-a]pyridin-7-yloxy)methyl)-6-azaspiro[3.4]octane-6-carboxylate (100 mg, 280 µmol) was dissolved in DCM (9 mL) followed by the addition of TFA (1 g, 0.01 mol). The reaction mixture was stirred for 1.5 h before being concentrated. SCX yielded the product (50 mg, 66 %) as an oil.

$[M+H]^+$ = 258.2

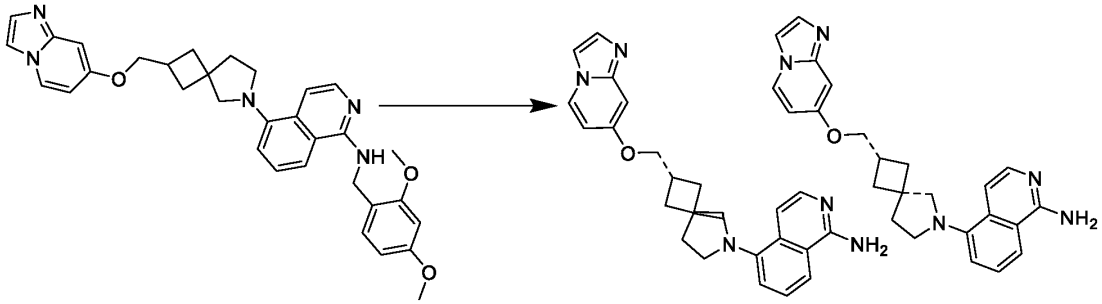
N-(2,4-Dimethoxybenzyl)-5-(2-((imidazo[1,2-a]yridine-7-yloxy)methyl)-6-azaspiro[3.4]octan-6-yl)isoquinolin-1-amine



According to a modification of General Method **4**, 7-((6-azaspiro[3.4]octan-2-yl)methoxy)imidazo[1,2-a]pyridine (50 mg,0.19 mmol) was reacted with 5-bromo-N-(2,4-dimethoxybenzyl)isoquinolin-1-amine (73 mg, 0.19 mmol), RuPhos Pd G3 (8.1 mg, 9.7 µmol) and NaO^tBu (37 mg, 0.39 mmol) in 1,4-dioxane (2 mL) at 80 °C for 18 h. Work up and SCX afforded the product (85 mg, 52% yield) as an oil.

$[M+H]^+$ = 550.2

5-(2-((Imidazo[1,2-a]pyridin-7-yloxy)methyl)-6-azaspiro[3.4]octan-6-yl)isoquinolin-1-amine (Examples 8806 and 8807)



According to a modification of General Method **8**, N-(2,4-dimethoxybenzyl)-5-(2-((imidazo[1,2-a]pyridin-7-yloxy)methyl)-6-azaspiro[3.4]octan-6-yl)isoquinolin-1-amine (85 mg, 0.12 mmol) was dissolved in DCM (9 mL) followed by the addition of TFA (1 mL). The reaction mixture was warmed to rt and stirred for 1.5 h before being concentrated. After SCX, purification by automated prep. HPLC (mass directed 20-100% over 12.5 min in basic mobile phase) afforded the trans* and cis* isomers.

Example 8806

^{1}H NMR (CD_3OD, 500 MHz) δ 2.09 (4H, td, J = 7.4, 3.9 Hz), 2.29 - 2.37 (2H, m), 2.82 (1H, tt, J = 8.5, 6.3 Hz), 3.42 (2H, t, J= 6.8 Hz), 3.51 (2H, s), 4.09 (2H, d, J = 6.4 Hz), 6.66 (1H, dd, J = 7.4, 2.4 Hz), 6.88 (1H, d, J = 2.5 Hz), 7.15 (1H, dd, J = 7.8,0.9 Hz), 7.31 (1H, dd, J = 6.3, 1.0 Hz), 7.36 - 7.44 (2H, m), 7.62 (1H, dt, J = 8.4, 1.0 Hz), 7.66 (1H, dd, J = 1.5, 0.7 Hz), 7.71(1H, d, J = 6.3 Hz), 8.28 (1H, dd, J = 7.4, 0.7 Hz)

$[M+H]^+$ = 400.2

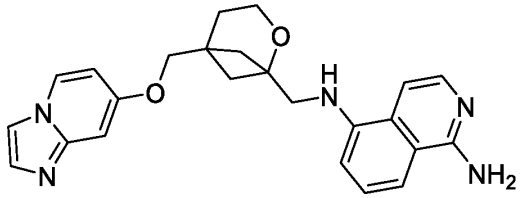
Example 8807

^{1}H NMR (CD_3OD, 500 MHz) δ 2.05 - 2.14 (2H, m), 2.18 (2H, t, J = 6.6 Hz), 2.22 - 2.30 (2H, m), 2.87 (1H, tt, J = 8.3, 6.1 Hz),3.43 (2H, s), 3.48 (2H, q, J = 7.2 Hz), 4.05 (2H, d, J = 6.2 Hz), 6.59 - 6.69 (1H, m), 6.85 (1H, d, J = 2.5 Hz), 7.11 (1H, dd, J =7.8, 0.9 Hz), 7.29 (1H, dd, J = 6.4, 1.0 Hz), 7.34 - 7.49 (2H, m), 7.59 (1H, dt, J = 8.4, 1.0 Hz), 7.61 - 7.73 (2H, m), 8.22 -8.31 (1H, m)

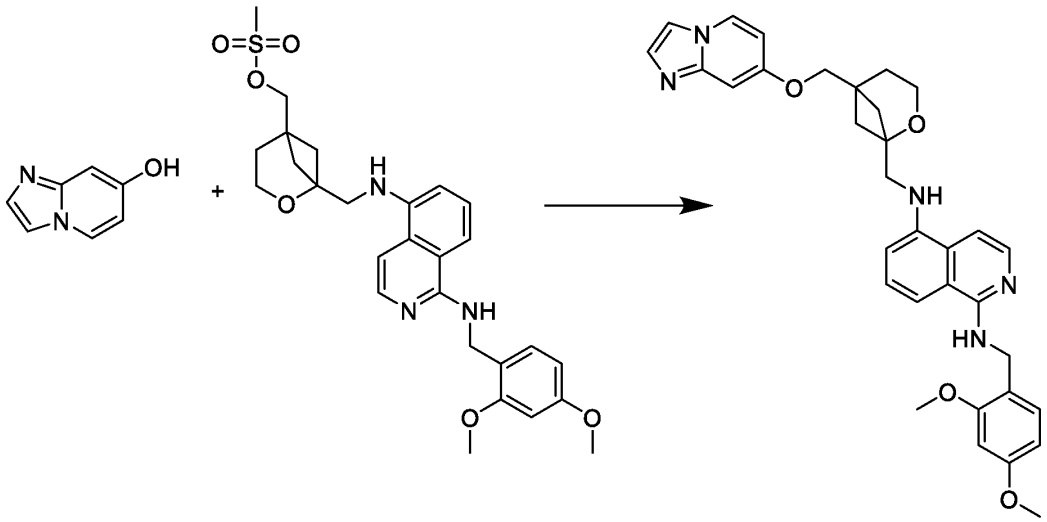
$[M+H]^+$ = 400.2

Example number 10901

N5-((5-((Imidazo[1,2-a]pyridin-7-yloxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine



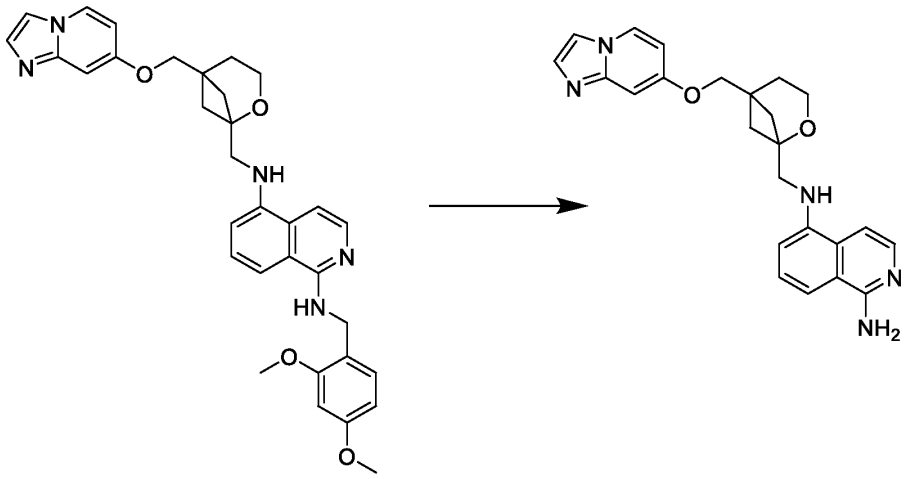
1-N-[(2,4-Dimethoxyphenyl)methyl]-5-N-[[5-(imidazo[1,2-a]pyridin-7-yloxymethyl)-2-oxabicyclo[3.1.1]heptan-1-yl]methyl]isoquinoline-1,5-diamine



Following General Method **2a**, imidazo[1,2-a]pyridin-7-ol hydrochloride (55 mg, 0.32 mmol) was reacted with[1-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-2-oxabicyclo[3.1.1]heptan-5-yl]methyl methanesulfonate (190 mg, 0.32 mmol) in DMF (4 mL) with NaH (32 mg, 0.81 mmol). The mixture was filtered through filter paper, washed with EtOAc (50 mL) and MeOH (10 mL) and the filtrate was concentrated by azeotroping with toluene. The residue was taken up in DCM and concentrated onto silica before being purified by flash chromatogrphy (Silica, 0-100% EtOAc in Pet. Ether followed by 0-20% MeOH in EtOAc) to afford the product (91 mg, 50% yield).

$[M+H]^+$ = 566.2

N5-((5-((Imidazo[1,2-a]pyridin-7-yloxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine (Example 10901)

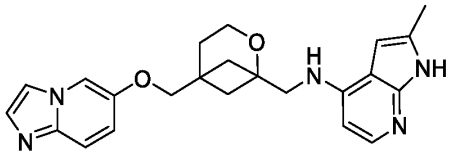


1-N-[(2,4-Dimethoxyphenyl)methyl]-5-N-[[5-(imidazo[1,2-a]pyridin-7-yloxymethyl)-2-oxabicyclo[3.1.1]heptan-1-yl]methyl]isoquinoline-1,5-diamine (91 mg, 0.16 mmol) was deprotected according to General Method **8**, in TFA (2601 µL, 33.76 mmol) at rt for 60 min. After SCX, lyophilisation afforded the product (52 mg, 78% yield) as a solid. $[M+H]^+$ = 416.2

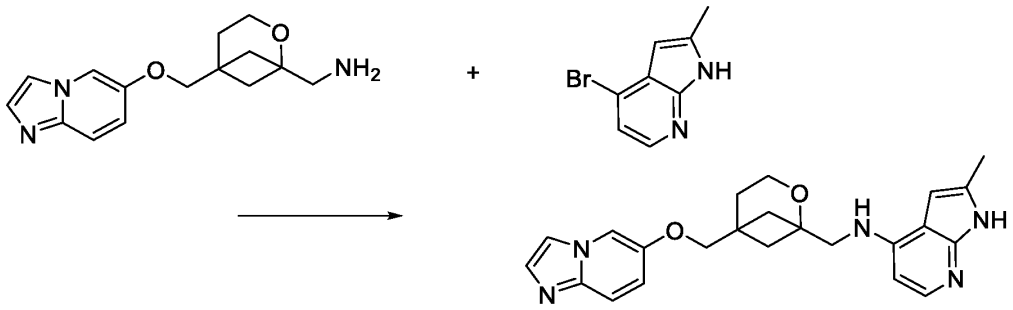
^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.03 (2H, dd, J = 8.4, 6.0 Hz), 2.09 (2H, td, J = 6.6, 5.8, 2.6 Hz), 2.15 (2H, t, J = 6.9 Hz), 3.32 (2H, d, J = 4.4 Hz), 3.86 (2H, s), 4.26 (2H, t, J = 6.8 Hz), 4.65 (1H, s), 5.13 (2H, s), 6.51 (1H, dd, J = 7.4, 2.5 Hz), 6.73 (1H, d, J = 7.7 Hz), 6.83 (1H, d, J = 2.4 Hz), 7.01 (1H, dd, J = 6.1, 1.0 Hz), 7.13 (1H, d, J = 8.3 Hz), 7.36 (1H, t, J = 8.0 Hz), 7.41 (1H, d, J = 1.2 Hz), 7.48 (1H, d, J = 1.4 Hz), 7.93 (2H, dd, J = 6.8, 3.8 Hz) ppm.

Example number 10907

N-[[5-(Imidazo[1,2-a]pyridin-7-yloxymethyl)-2-oxabicyclo[3.1.1]heptan-1-yl]methyl]-2-methyl-1H-pyrrolo[2,3-b]pyridin-4-amine



N-[[5-(Imidazo[1,2-a]pyridin-7-yloxymethyl)-2-oxabicyclo[3.1.1]heptan-1-yl]methyl]-2-methyl-1H-pyrrolo[2,3-b]pyridin-4-amine (Example 10907)



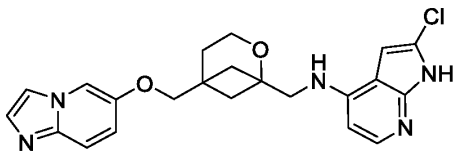
According to a modification of General Method **4**, [[5-(imidazo[1,2-a]pyridin-7-yloxymethyl)-2-oxabicyclo[3.1.1]heptan-1-yl]methanamine (135 mg, 0.37 mmol) was reacted with 4-bromo-2-methyl-1H-pyrrolo[2,3-b]pyridine (77.0 mg, 0.37 mmol) in THF (5 mL) in the presence of LiHMDS (1M in THF) (183 µl, 1.83 mmol) and Brettphos Pd G3 (17 mg, 0.02 mmol) at 60 °C in a sealed vial for 6 days. The product was purified by flash chromatography (Silica, 0-100% EtOAc in Pet. ether followed by 0-15% MeOH in EtOAc) followed by automated prep HPLC (mass directed 2-60% over 20 min in basic mobile phase) and lyophilised to afford the product (22.0 mg, 15% yield).

$[M+H]^+$ = 404.2

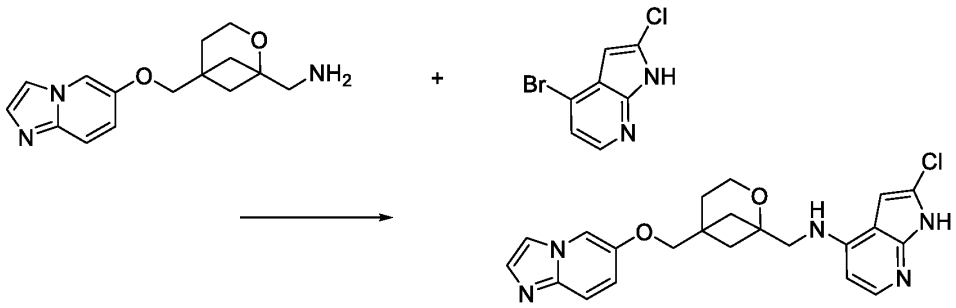
^{1}H NMR (DMSO-d_6, 400 MHz) δ 1.80 (2H, dd, J = 7.0, 2.5 Hz), 1.95 (2H, d, J = 7.8 Hz), 2.02 (2H, t, J = 6.8 Hz), 2.30 (3H, d, J = 1.0 Hz), 3.25 (2H, d, J = 6.2 Hz), 3.86 (2H, s), 4.07 (2H, t, J = 6.8 Hz), 6.09 (1H, d, J = 5.6 Hz), 6.14 (1H, t, J = 6.2 Hz), 6.25 (1H, dd, J = 2.1, 1.1 Hz), 6.51 (1H, dd, J = 7.4, 2.5 Hz), 6.87 (1H, d, J = 2.5 Hz), 7.35 (1H, d, J = 1.3 Hz), 7.68 (1H, d, J = 5.5 Hz), 7.71 (1H, dd, J = 1.3, 0.7 Hz), 8.34 (1H, dd, J = 7.4, 0.7 Hz), 10.91 (1H, s)

Example number 10909

2-Chloro-N-[[5-(imidazo[1,2-a]pyridin-6-yloxymethyl)-2-oxabicyclo[3.1.1]heptan-1-yl]methyl]-1H-pyrrolo[2,3-b]pyridin-4-amine



2-Chloro-N-[[5-(imidazo[1,2-a]pyridin-6-yloxymethyl)-2-oxabicyclo[3.1.1]heptan-1-yl]methyl]-1H-pyrrolo[2,3-b]pyridin-4-amine (Example 10909)



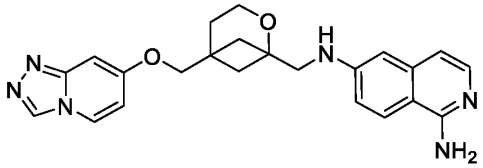
According to a modification of General Method **4,** [5-(imidazo[1,2-a]pyridin-6-yloxymethyl)-2-oxabicyclo[3.1.1]heptan-1-yl]methanamine (26.0 mg, 0.1 mmol) was reacted with 4-bromo-2-chloro-1H-pyrrolo[2,3-b]pyridine (20.0 mg, 0.09 mmol) in THF (5 mL) in the presence of Brettphos Pd G3 (4 mg) and LiHMDS (1M in THF) (207 µL, 0.21 mmol) at 70 °C for 5 h. After work up and SCX the residue was purified by flash chromatography (Silica, 0 - 24% (10% NH_3 in MeOH) in DCM) and lyophilised to afford the product (4 mg, 8% yield).

$[M+H]^+$ = 424.1

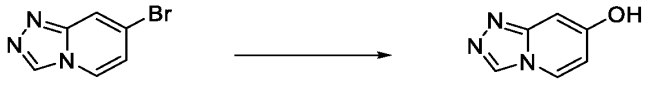
^1H NMR (CD_3CN) δ 1.82 (2H, dd, J = 7.2, 2.4 Hz), 1.89 - 1.92 (2H, m), 2.00 (2H, t, J = 6.8 Hz), 3.26 (2H, d, J = 6.0 Hz), 3.71 (2H, s), 4.05 (2H, t, J = 6.8 Hz), 4.99 (1H, s), 5.16 (1H, t, J = 5.8 Hz), 6.19 (1H, t, J = 6.0 Hz), 6.35 (1H, s), 6.86 (1H, dd, J = 9.8, 2.3 Hz), 7.31 (1H, d, J = 9.7 Hz), 7.38 (1H, d, J = 0.8 Hz), 7.55 (1H, s), 7.77 (1H, J = 5.7 Hz), 7.82 (1H, d, J = 2.0 Hz)

Example number 10926

5-N-[[5-([1,2,4]Triazolo[4,3-a]pyridin-7-yloxymethyl)-2-oxabicyclo[3.1.1]heptan-1-yl]methyl]isoquinoline-1,5-diamine



[1,2,4]Triazolo[4,3-a]pyridin-7-ol



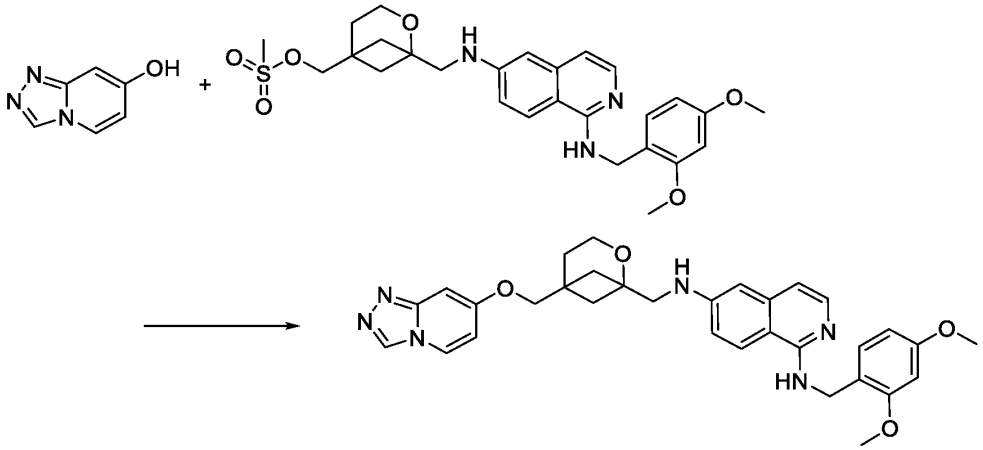
According to a modification of General Method **13,** 7-bromo[1,2,4]triazolo[4,3-a]pyridine (525 mg, 2.65 mmol) was reacted with 4,4,5,5-tetramethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3,2-dioxaborolane (1.52 g, 5.97 mmol) at 100 °C for 2 h. The mixture was cooled to 0 °C and 30 w% H_2O_2 (542

µL, 5.3 mmol) was added dropwise. The mixture was stirred for 5 h at rt. Work up followed by SCX afforded the product (140 mg, 27% yield).

$[M+H]^+$ = 136.0

^{1}H NMR (d6-DMSO, 400 MHz) δ 6.61 (1H, dd, J = 7.5, 2.1 Hz), 6.73 (1H, d, J + 1.8 Hz), 8.38 (1H, d, J = 7.3 Hz), 8.98 (1H, s), OH proton not seen

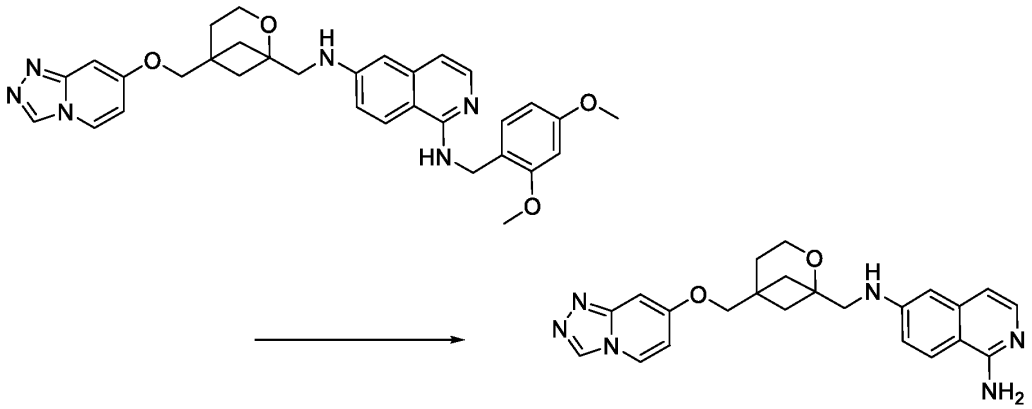
1-N-[(2,4-Dimethoxyphenyl)methyl]-5-N-[[5-([1,2,4]triazolo[4,3-a]pyridin-7-yloxymethyl)-2-oxabicyclo[3.1.1]heptan-1-yl]methyl]isoquinoline-1,5-diamine



According to a modification of General Method **2b**, to a mixture of [1,2,4]triazolo[4,3-a]pyridin-7-ol (80 mg, 0.41 mmol) and [1-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-2-oxabicyclo[3.1.1]heptan-5-yl]methyl methanesulfonate (219 mg, 0.41 mmol) in DMSO (1 mL) was added K_2CO_3 325 mesh (172 mg, 1.24 mmol). The mixture was heated under nitrogen at 100 °C for 30 min. The mixture was partitioned between EtOAc (50 mL) and water (25 mL). The organic layer was washed with water (4 x 20 mL), dried ($MgSO_4$) and concentrated. The product was purified by flash chromatography (Silica, 0-100% EtOAc in Pet. Ether followed by 0-20% MeOH in EtOAc) to afford the product (120 mg, 46% yield)

$[M+H]^+$ = 567.3

5-N-[[5-([1,2,4]Triazolo[4,3-a]pyridin-7-yloxymethyl)-2-oxabicyclo[3.1.1]heptan-1-yl]methyl]isoquinoline-1,5-diamine (Example 10926)



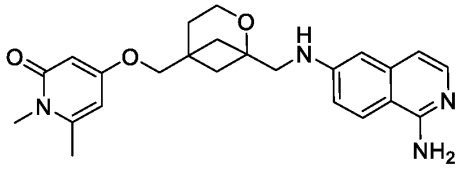
According to a modification of General Method **8**, a solution of 1-N-[(2,4-dimethoxyphenyl)methyl]-5-N-[[5-([1,2,4]triazolo[4,3-a]pyridin-7-yloxymethyl)-2-oxabicyclo[3.1.1]heptan-1-yl]methyl]isoquinoline-1,5-diamine (120 mg, 0.19 mmol) in DCM (1 mL) was treated with TFA (2.70 mL, 35.0mmol), stirred at rt for 4 h and the mixture concentrated. The residue was taken up in MeOH (2 mL), loaded on to a 2 g SCX-2 column, flushed with MeOH (15 mL), followed by 1M NH_3 in MeOH (15 mL). The latter was concentrated and purified by flash chromatography (Silica, 0-100% EtOAc in Pet. Ether followed by 0-50% MeOH in EtOAc) and lyophilized to afford the product (66 mg, 83% yield).

$[M+H]^+$ = 417.2

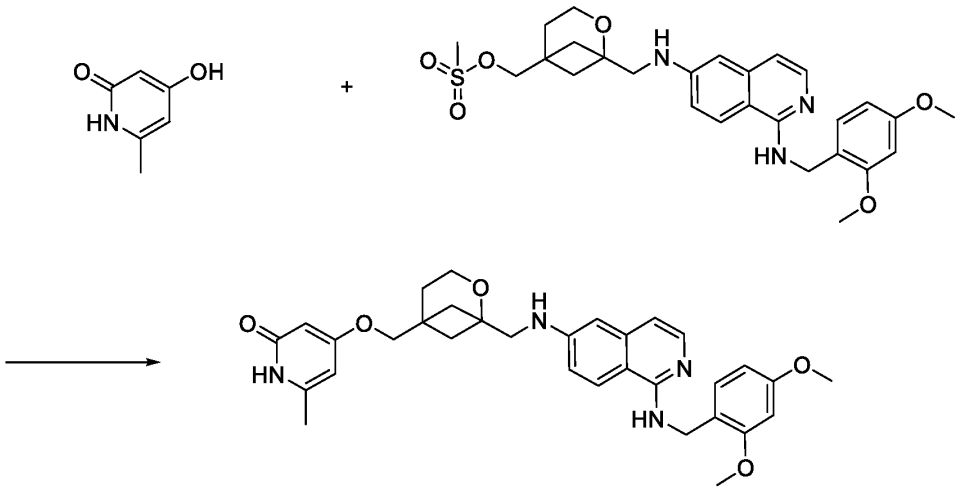
^{1}H (DMSO-d_6, 400 MHz) δ 1.85 (2H, dd, J = 7.1, 2.1 Hz), 1.97 (2H, d, J = 8.8 Hz), 2.04 (2H, t, J = 6.8 Hz), 3.24 (2H, d, J = 5.7 Hz), 3.93 (2H, s), 4.10 (2H, t, J = 6.8 Hz), 5.78 (1H, t, J = 5.8 Hz), 6.52 (2H, s), 6.59 (1H, dd, J = 7.4, 2.2 Hz), 6.64 (1H, d, J = 7.7 Hz), 7.02 (1H, d, J = 2.2 Hz), 7.11 (1H, d, J = 6.1 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.73 (1H, d, J = 6.1 Hz), 8.38 (1H, d, J = 7.5 Hz), 8.45 (1H, s)

Example number 10928

4-((1-(((1-Aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[3.1.1]heptan-5-yl)methoxy)-1,6-dimethylpyridin-2(1H)-one



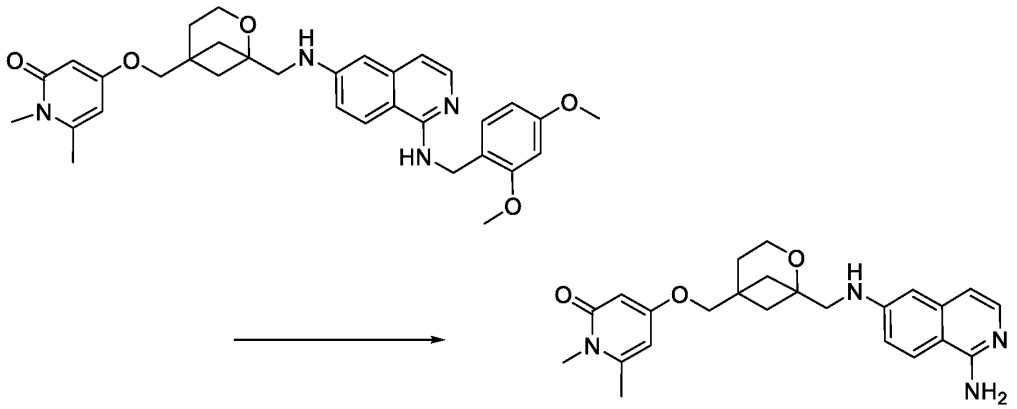
4-((1-(((1-((2,4-Dimethoxybenzyl)amino)isoquinolin-5-yl)amino)methyl)-2- oxabicyclo[3.1.1]heptan-5-yl)methoxy)-1,6-dimethylpyridin-2(1H)-one



According to a modification of General Method **2b**, [1-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-2-oxabicyclo[3.1.1]heptan-5-yl]methyl methanesulfonate, (150 mg, 284 µmol) was dissolved in DMF (5 mL) followed by the addition of 4-hydroxy-1,6-dimethylpyridin-2(1H)-one (59.3 mg, 426 µmol)and K_2CO_3 (118 mg, 853 µmol). The reaction mixture was then heated to 60 °C and stirred for 18 h. The reaction mixture was allowed to cool to rt and was quenched by the addition of water (30 mL). The mixture was then diluted with EtOAc (30 mL) and the aq phase extracted with EtOAc (2 x 30 mL). The combined organic phase was washed sequentially with sat. aq $NaHCO_3$, water and Brine (30 mL each) before being dried over $MgSO_4$, filtered and concentrated. The product was purified by chromatography (Silica, 0-20% (0.7 M NH_3/MeOH)/DCM) to afford the product (50 mg, 28 % yield)

^{1}H NMR (CDCl3, 500 MHz) δ 1.22 - 1.33 (2H, m), 1.91 - 1.97 (2H, m), 1.98 - 2.10 (4H, m), 2.27 (3H, s), 3.27 (2H, s), 3.43 (3H, s), 3.47 (1H, s), 3.79 (3H, s), 3.85 (3H, s), 4.21 (2H, t, J = 6.8 Hz), 4.60 (1H, s), 4.74 (2H, d, J = 5.2 Hz), 5.77 (2H, d, J = 1.5 Hz), 6.44 (1H, dd, J = 8.3, 2.4 Hz), 6.49 (1H, d, J = 2.4 Hz), 6.68 (1H, d, J = 7.7 Hz), 6.87 (1H, d, J = 6.2 Hz), 7.07 (1H, d, J = 8.4 Hz), 7.28 (1H, t, J = 8.0 Hz), 7.32 (1H, d, J = 8.2 Hz), 7.99 (1H, d, J = 6.2 Hz)

4-((1-(((1-Aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[3.1.1]heptan-5-yl)methoxy)-1,6-dimethylpyridin-2(1H)-one (Example 10928)



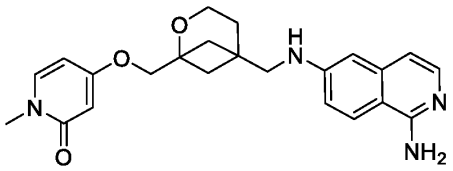
According to a modification of general Method **8**, 4-((1-(((1-((2,4-dimethoxybenzyl)amino)isoquinolin-5-yl)amino)methyl)-2-oxabicyclo[3.1.1]heptan-5-yl)methoxy)-1,6-dimethylpyridin-2(1H)-one (50 mg, 88 µmol) was dissolved in DCM (9 mL) followed by the addition of TFA (1 g, 0.01 mol). The reaction mixture was heated to 40 °C and stirred for 1 h and then concentrated. The material was dissolved in MeOH (2 mL) and passed over an SCX column, eluting in 2.5 M NH3 in MeOH (25 mL). Product-containing eluent was concentrated and lyophilized to afford the product (28 mg, 97% yield).

$[M+H]^+$ = 421.2

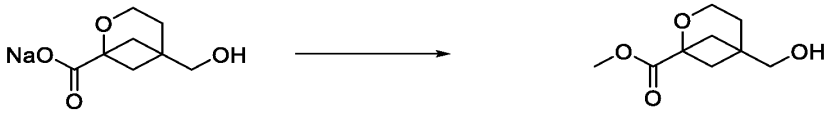
^{1}H NMR (DMSO, 500 MHz) δ 1.75 - 1.86 (2H, m), 1.91 (2H, dt, J = 8.4, 4.2 Hz), 1.96 (2H, t, J = 6.9 Hz), 2.25 (3H, s), 3.22 (2H, d, J = 5.9 Hz), 3.29 (3H, s), 3.74 (2H, s), 4.06 (2H, t, J = 6.8 Hz), 5.64 (1H, d, J = 2.8 Hz), 5.73 - 5.81 (2H, m), 6.64 - 6.71 (3H, m), 7.13 (1H, d, J = 6.3 Hz), 7.23 (1H, t, J = 8.0 Hz), 7.35 (1H, d, J = 8.3 Hz), 7.71 (1H, d, J = 6.2 Hz)

Example Number 11101

4-[[5-[[(1-Aminoisoquinolin-5-yl)amino]methyl]-2-oxabicyclo[3.1.1]heptan-1-yl]methoxy]-1-methylpyridin-2-one



Methyl 5-(hydroxymethyl)-2-oxabicyclo[3.1.1]heptane-1-carboxylate

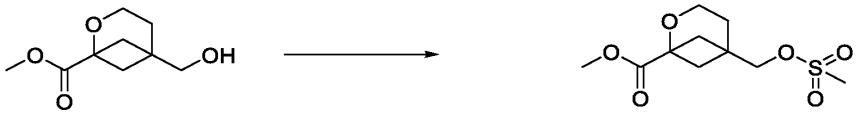


To a stirred suspension of 5-(hydroxymethyl)-2-oxabicyclo[3.1.1]heptane-1-carboxylic acid sodium salt (600 mg, 2.8 mmol) in MeOH (4 mL) in an ice bath was added thionyl chloride (816 µL, 11.19 mmol) dropwise. The reaction was allowed to warm to rt and stirred for 22 h. The reaction mixture was diluted with DCM (40 mL) and washed with water (20 mL). The aq layer was back extracted with DCM (30 mL). The combined organic fractions were dried (Na_2SO_4) and concentrated to afford the product (409 mg, 71% yield).

$[M+H]^+$ = 187.1

^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.94 - 2.05 (4H, m), 2.33 (2H, ddt, J = 7.2, 2.3, 1.0 Hz), 3.54 (2H, s), 3.77 (3H, s), 4.19-4.27 (2H,m), OH not seen.

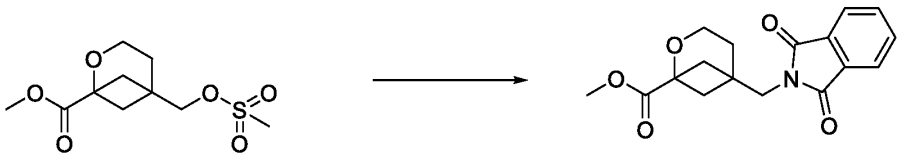
Methyl 5-(methylsulfonyloxymethyl)-2-oxabicyclo[3.1.1]heptane-1-carboxylate



According to a modification of the General Method **1a**, a solution of methyl 5-(hydroxymethyl)-2-oxabicyclo[3.1.1]heptane-1-carboxylate (404 mg, 1.95 mmol) and TEA (544 µL, 3.91 mmol) in DCM (5 mL) was cooled to 0 °C and MsCl (227 µL, 2.93 mmol) was added to the mixture and the reaction was allowed to warm to rt and stir for 22 h. The mixture was washed with water (20 mL) and the aq phase was extracted with DCM (30 ml). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated in to afford the product (372 mg, 58% yield).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.05 - 2.13 (4H, m), 2.35 - 2.44 (2H, m), 3.05 (3H, s), 3.78 (3H, s), 4.12 (2H, s), 4.19 - 4.26 (2H, m)

Methyl 5-[(1,3-dioxoisoindol-2-yl)methyl]-2-oxabicyclo[3.1.1]heptane-1-carboxylate



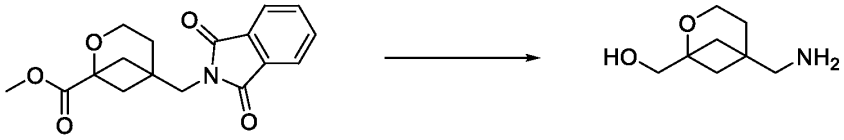
A suspension of methyl 5-(methylsulfonyloxymethyl)-2-oxabicyclo[3.1.1]heptane-1-carboxylate (100 mg, 0.303 mmol) and potassium phthalimide (62.0 mg, 0.333 mmol) in DMF (4 mL) was stirred at 100 °C for 3 h. The mixture was cooled to rt, taken up in water (20 mL) and washed with EtOAc (2x30 mL). The

combined organic layers were washed with brine (10 mL), dried (Na_2SO_4) and concentrated to afford the product (98 mg, 82% yield).

$[M+H]^+$ = 316.0

^1H NMR ($CDCl_3$, 400 MHz) δ 2.01 - 2.14 (4H, m), 2.30 - 2.39 (2H, m), 3.73 (5H, s), 4.15 - 4.21 (2H, m), 7.71 - 7.79 (2H, m), 7.83 - 7.90 (2H, m)

[5-(Aminomethyl)-2-oxabicyclo[3.1.1]heptan-1-yl]methanol

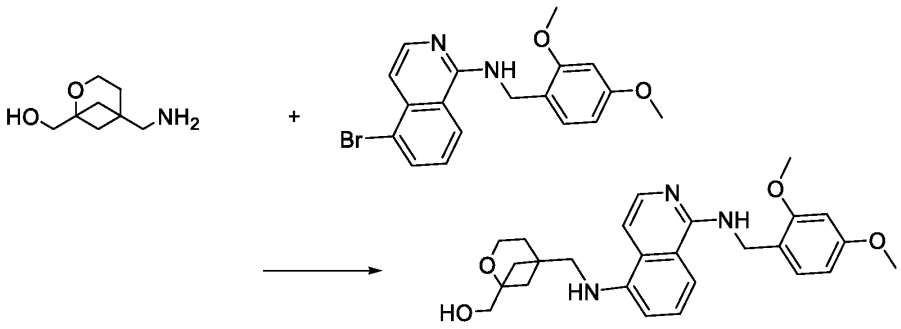


To a stirred solution of methyl 5-[(1,3-dioxoisoindol-2-yl)methyl]-2-oxabicyclo[3.1.1]heptane-1-carboxylate (98 mg, 0.25 mmol) in IPA (4 mL) and water (1 mL), was added sodium borohydride (56 mg, 1.49 mmol). After stirring for 24 h, AcOH (256 µL, 4.48 mmol) was added slowly and when the foaming subsided, the reaction was heated to 80°C for 22 h. The reaction mixture was concentrated, the residue taken up in MeOH (1 mL) and the mixture was passed directly through an SCX and washed with MeOH. The product was eluted with a solution of 1M NH_3 in MeOH and concentrated to afford the product (39 mg, 100% yield).

$[M+H]^+$ = 158.1

^1H NMR ($CDCl_3$, 400 MHz) δ 1.60 - 1.67 (2H, m), 1.82 (2H, dd, J = 7.2, 2.7 Hz), 1.92 - 1.98 (2H, m), 2.64 (2H, s), 3.51 (2H, s), 4.07 - 4.16 (2H, m) three exchangeable protons are not observed.

[5-[[[1-[(2,4-Dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-2-oxabicyclo[3.1.1]heptan-1-yl]methanol

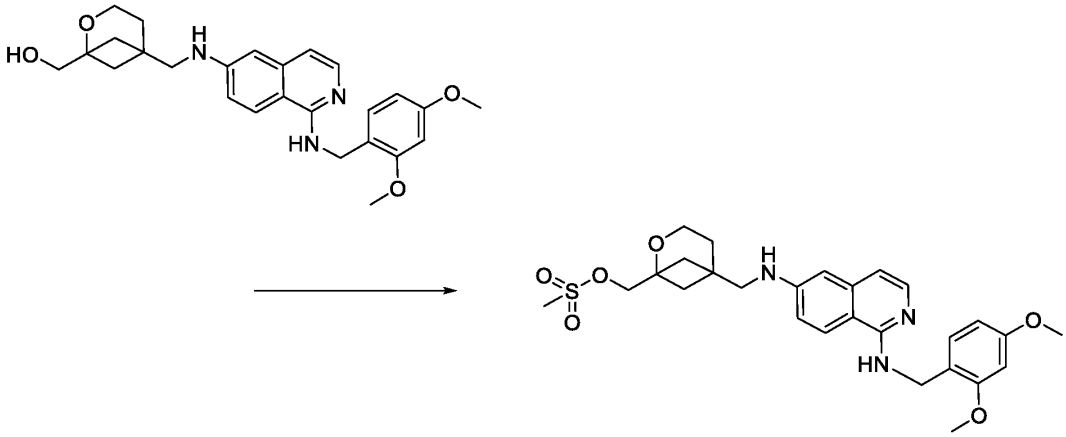


According to a modification of General Method **4**, a suspension of [5-(aminomethyl)-2-oxabicyclo[3.1.1]heptan-1-yl]methanol (40 mg, 0.25 mmol), 5-bromo-N-[(2,4-

dimethoxyphenyl)methyl]isoquinolin-1-amine (104 mg, 0.28 mmol) and NaO^{t}Bu (37 mg, 0.38 mmol) in 1,4-dioxane (5 mL) was purged with N_2(g) for 5 min. Brettphos Pd G4 (23 mg, 0.03 mmol) was added and the mixture purged for a further 5 min with N_2(g). The mixture was stirred in a sealed vial at 40 °C for 20 h and at 60 °C for another 18 h. The reaction was cooled and concentrated. The residue was purified by flash chromatography (Silica, 0-100% EtOAc in Pet. Ether followed by 0-5% MeOH in EtOAc) to afford the product (23 mg, 20% yield).

$[M+H]^+$ = 450.4

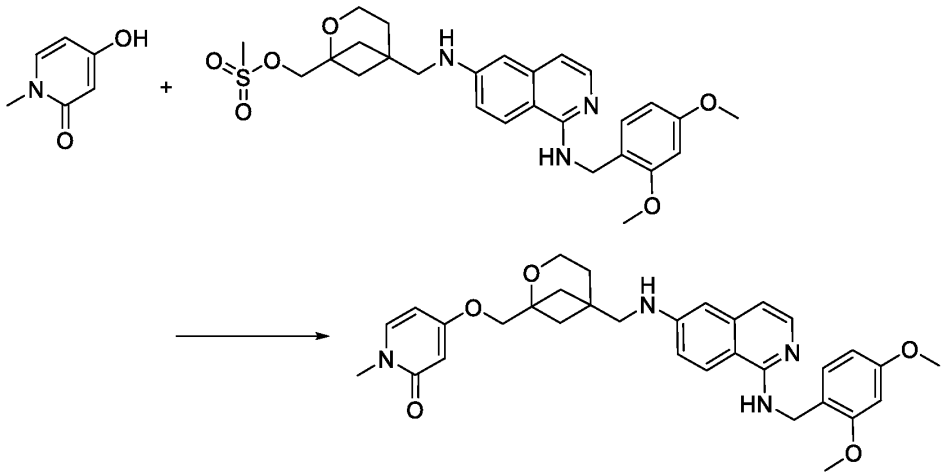
[5-[[[1-[(2,4-Dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-2-oxabicyclo[3.1.1]heptan-1-yl]methyl methanesulfonate



According to a modification of General Method **1a**, a solution of [5-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-2-oxabicyclo[3.1.1]heptan-1-yl]methanol (23 mg, 0.05 mmol) and TEA (14 µL, 0.1 mmol) in DCM (4 mL) was cooled in an ice/water bath. MsCl (8 µL, 0.1 mmol) was added dropwise maintaining the temperature at 0 °C. The mixture was stirred 0 °C for 60 min after which time it was allowed to warm to rt and stirred for 3 days. The mixture was quenched with water (30 mL) and washed with DCM (2 x 50 mL), dried (Na_2SO_4) and concentrated to afford the product (40 mg, 99% yield).

$[M+H]^+$ = 528.5

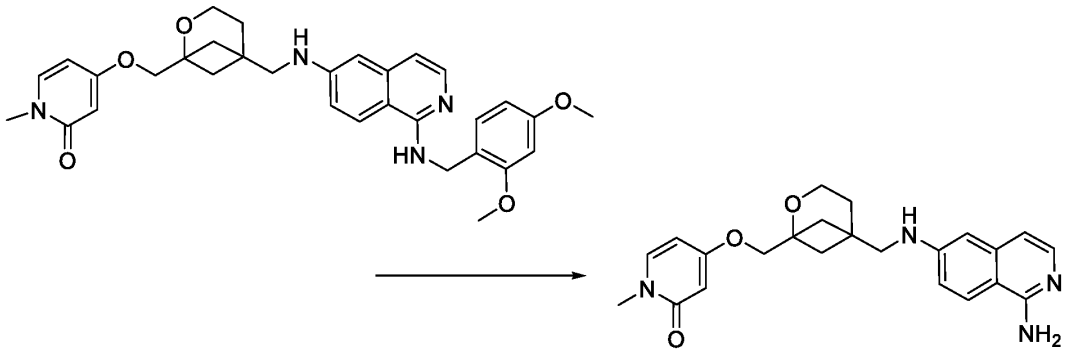
4-[[5-[[[1-[(2,4-Dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-2-oxabicyclo[3.1.1]heptan-1-yl]methoxy]-1-methylpyridin-2-one



According to a modification of General Method **2b**, to a mixture of [5-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-2-oxabicyclo[3.1.1]heptan-1-yl]methyl methanesulfonate (40 mg, 0.05 mmol) and $CsCO_3$ (50 mg, 0.15 mmol) in MeCN (5 mL) was added 4-hydroxy-1-methyl-2-pyridone (10 mg, 0.08 mmol). The mixture was heated at 60 °C for 20 h. The mixture was cooled, filtered, washed with EtOAc:MeOH 5:1 (20 mL) and the filtrate was concentrated to afford the product (90 mg, 91% yield).

$[M+H]^+$ = 557.6

4-[[5-[[(1-Aminoisoquinolin-5-yl)amino]methyl]-2-oxabicyclo[3.1.1]heptan-1-yl]methoxy]-1-methylpyridin-2-one (Example 11101)



According to a modification of General Method **8**, 4-[[5-[[[1-[(2,4-dimethoxyphenyl)methylamino]isoquinolin-5-yl]amino]methyl]-2-oxabicyclo[3.1.1]heptan-1-yl]methoxy]-1-methylpyridin-2-one (90 mg, 0.06 mmol) was taken up in TFA (990 µL, 12.9 mmol) and stirred at 40 °C for 30 min. After removal of TFA, the residue was suspended in MeOH (2ml) and loaded

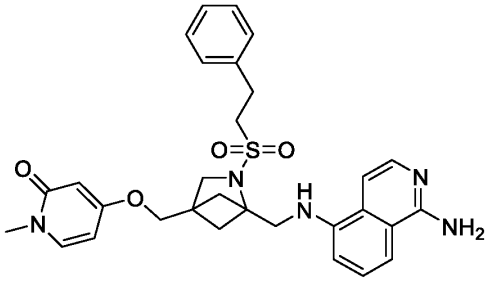
on to a 2 g SCX-2 column, which was flushed with MeOH (10 mL), followed by 3.5 M NH_3 in MeOH (15 mL) to elute the product. Purification by automated prep HPLC (mass directed 2-60% over 20 min in basic mobile phase) afforded the product (5 mg, 19% yield).

$[M+H]^+$ = 407.4

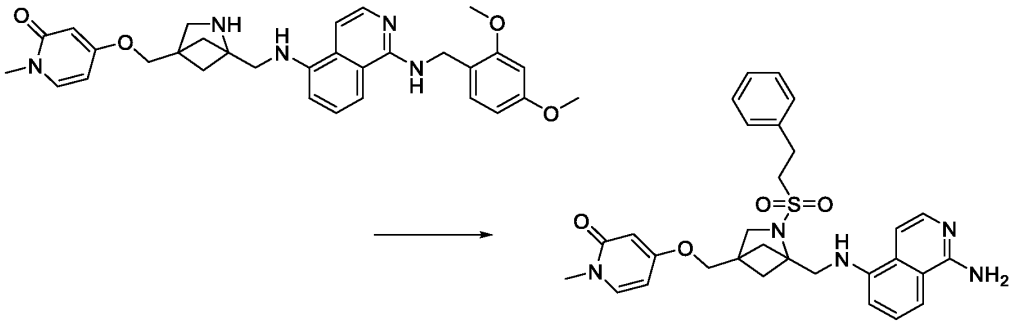
^{1}H NMR (DMSO-d_6, 400 MHz) δ 1.77 - 1.84 (2H, m), 1.87 - 1.95 (2H, m), 2.02 (2H, t, J = 6.9 Hz), 3.18 (2H, d, J = 5.8 Hz), 3.30 (3H, s), 3.79 (2H, s), 4.02 (2H, t, J = 6.8 Hz), 5.72 (1H, d, J = 2.8 Hz), 5.85 (1H, dd, J = 7.5, 2.7 Hz), 5.89 (1H, t, J = 6.0 Hz), 6.45 - 6.52 (2H, m), 6.61 (1H, d, J = 7.7 Hz), 7.16 - 7.22 (2H, m), 7.31 (1H, d, J = 8.3 Hz), 7.51 (1H, d, J = 7.5 Hz), 7.72 (1H, d, J = 6.1 Hz)

Example Number 12014

4-((1-(((1-Aminoisoquinolin-5-yl)amino)methyl)-2-(phenethylsulfonyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one



4-[[1-[[(1-aminoisoquinolin-5-yl)amino]methyl]-2-(2-phenylethylsulfonyl)-2-azabicyclo[2.1.1]hexan-4-yl]methoxy]-1-methylpyridin-2-one (Example 12014)



To a solution of 4-[[4-[[[1-[(2,4-dimethoxyphenyl)methylamino]-5-isoquinolyl]amino]methyl]-2-azabicyclo[2.1.1]hexan-1-yl]methoxy]-1-methyl-pyridin-2-one (68 mg, 0.126 mmol) and TEA (40 µL, 0.289 mmol) in anhydrous DCM (2mL) at 0 °C was added 2-phenylethanesulfonyl chloride (51.4 mg, 0.251 mmol). The mixture was stirred at 0 °C for 2 h and concentrated. The residue was taken up in in anhydrous DCM (2 mL) at rt and according to a variation of General Method **8,** TFA (811 µL, 10.9 mmol) was added. The mixture was stirred at rt for 2.5 h and concentrated. The residue was purified by flash chromatography

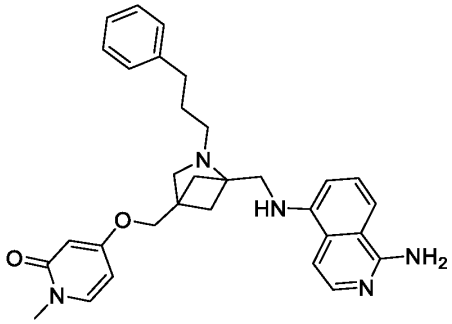
(Silica-C18, 0-80% MeCN in water [10 mM NH_4HCO_3]) followed by automated prep HPLC (mass directed, 35-45% MeCN in water [10 mM NH_4HCO_3]) and lyophilized to afford the product.

$[M+H]^+$ = 560.2

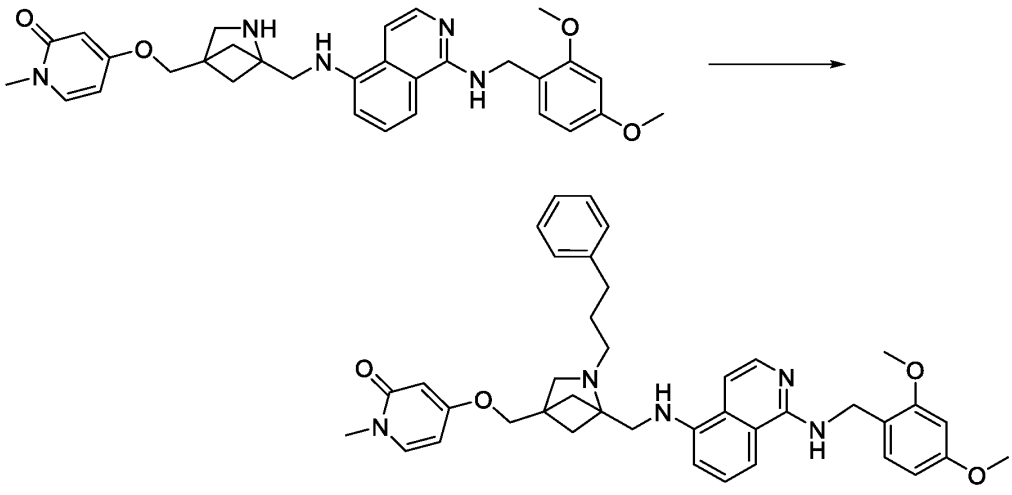
^{1}H NMR (500 MHz, DMSO-d6) δ 1.65 (2H, dd, J = 4.8, 1.9 Hz), 1.86 – 1.93 (2H, m), 3.04 – 3.11 (2H, m), 3.31 (3H, s), 3.45 – 3.49 (4H,m), 3.81 (2h, d, J = 6.1 Hz), 4.14 (2H, s), 5.78 (1H, d, J = 2.7 Hz), 5.86 – 5.93 (2h, m),6.53 (2h, d, J = 5.3 Hz), 6.69 (1H, d, J = 7.7 Hz), 6.99 – 7.04 (1h, m), 7.22 – 7.29 (6H, m), 7.37 (1H, d, J = 8.3 Hz), 7.53 (1H, d, J = 7.6 Hz), 7.74 (1H, d, J = 6.1 Hz)

Example Number 12019

4-((1-(((1-Aminoisoquinolin-5-yl)amino)methyl)-2-(3-phenylpropyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one



4-((1-(((1-((2,4-Dimethoxybenzyl)amino)isoquinolin-5-yl)amino)methyl)-2-(3-phenylpropyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one

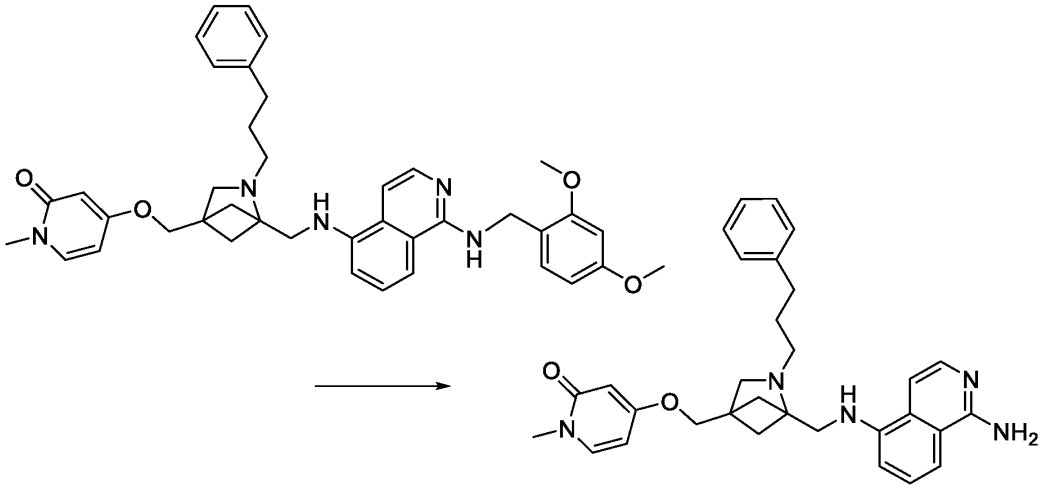


3-Phenylpropanal (22 mg, 0.16 mmol) was added to a mixture of 4-[[4-[[[1-[(2,4-dimethoxyphenyl)methylamino]-5-isoquinolyl]amino]methyl]-2-azabicyclo[2.1.1]hexan-1-yl]methoxy]-1-

methyl-pyridin-2-one (75 mg, 0.14 mmol) and AcOH (12 µL, 0.21 mmol) in dichloroethane (1.5 mL). The mixture was stirred at rt for 30 min then STAB (73 mg, 0.34 mmol) was added. The mixture was stirred at rt for 30 min. The reaction was quenched with sat. $NaHCO_3$(aq) (5 mL) and extracted with DCM (3 x 2 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Flash chromatography (Silica, 0-40% MeOH in EtOAc) afforded the product (79 mg, 87% yield).

$[M+H]^+$ = 660.5

4-((1-(((1-Aminoisoquinolin-5-yl)amino)methyl)-2-(3-phenylpropyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one (Example 12019)



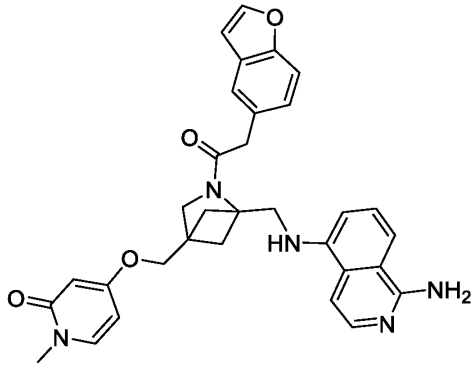
4-((1-(((1-((2,4-Dimethoxybenzyl)amino)isoquinolin-5-yl)amino)methyl)-2-(3-phenylpropyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one (79 mg, 0.120 mmol) was deprotected according to General Method **8** in TFA (178 µL, 2.39 mmol) and DCM (1200 µL) at rt for 1 h. The crude product was purified by flash chromatography (Silica-C18, 10-30% MeCN in water [10 mM NH_4HCO_3]). The product was loaded onto a PL-HCO_3 MP SPE cartridge (250 mg) eluting with a mixture of MeOH and MeCN (1:1, 5 mL). The filtrate was concentrated, and lyophilisation afforded the product (16 mg, 26%).

$[M+H]^+$ = 510.4

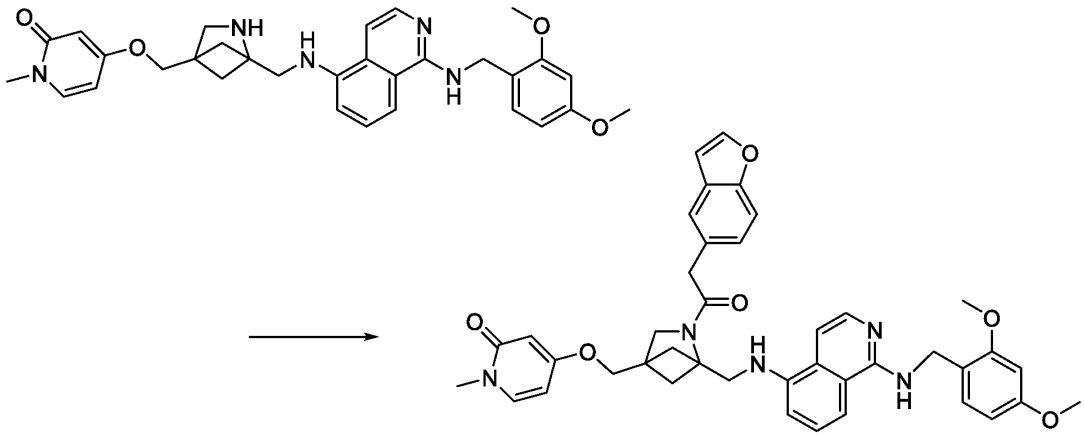
^{1}H NMR (DMSO-d6, 500 MHz) δ 1.61 (4H, q, J = 5.9 Hz), 1.72 (2H, p, J = 7.1 Hz), 2.52 (2H, d, J = 5.7 Hz), 2.64 - 2.68 (2H, m), 2.72 (2H, s), 3.31 (3H, s), 3.36 (2H, d, J = 5.2 Hz), 4.09 (2H, s), 5.58 (1H, t, J = 5.3 Hz), 5.76 (1H, d, J = 2.8 Hz), 5.89 (1H, dd, J = 7.5, 2.8 Hz), 6.52 (2H, s), 6.57 (1H, d, J = 7.7 Hz), 6.98 (1H, d, J = 5.9 Hz), 7.09 - 7.14 (1H, m), 7.15 - 7.24 (5H, m), 7.35 (1H, d, J = 8.4 Hz), 7.52 (1H, d, J = 7.6 Hz), 7.73 (1H, d, J = 6.1 Hz).

Example Number 12034

4-((1-(((1-Aminoisoquinolin-5-yl)amino)methyl)-2-(2-(benzofuran-5-yl)acetyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one



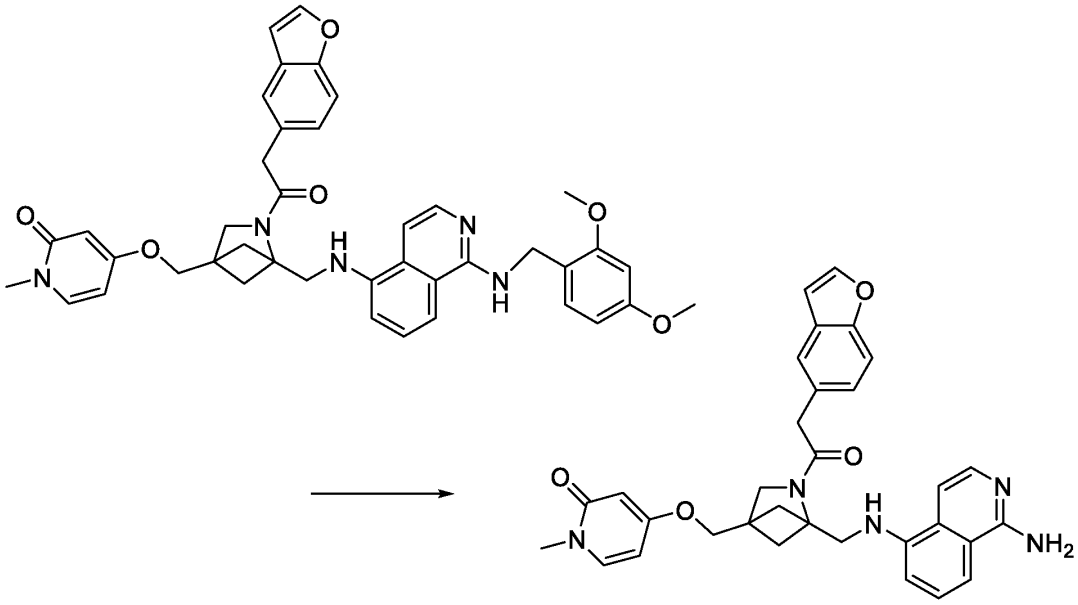
4-[[2-[2-(Benzofuran-5-yl)acetyl]-1-[[[1-[(2,4-dimethoxyphenyl)methylamino]-5-isoquinolyl]amino]methyl]-2-azabicyclo[2.1.1]hexan-4-yl]methoxy]-1-methyl-pyridin-2-one



To a solution of 4-[[4-[[[1-[(2,4-dimethoxyphenyl)methylamino]-5-isoquinolyl]amino]methyl]-2-azabicyclo[2.1.1]hexan-1-yl]methoxy]-1-methyl-pyridin-2-one (100 mg, 0.185 mmol) in DCM (2 mL) were added 2-(benzofuran-5-yl)acetic acid (32.5 mg, 0.185 mmol), HATU (77.2 mg, 0.203 mmol) and DIPEA (104 µL, 0.609 mmol). The mixture was stirred at rt for 16 h then diluted with DCM (10 mL), washed with water (3 x 10 mL), dried ($MgSO_4$) and concentrated to afford the product.

[M+H]+ = 700.0

4-((1-(((1-Aminoisoquinolin-5-yl)amino)methyl)-2-(2-(benzofuran-5-yl)acetyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one (Example 12034)



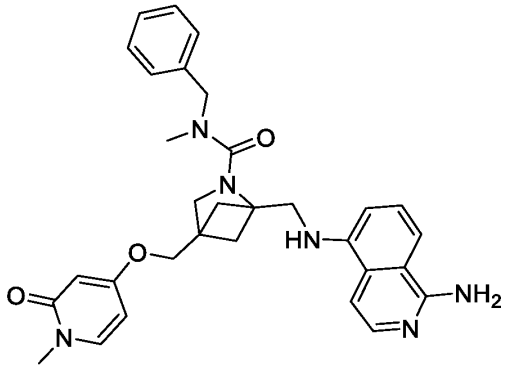
4-[[2-[2-(Benzofuran-5-yl)acetyl]-1-[[[1-[(2,4-dimethoxyphenyl)methylamino]-5-isoquinolyl]amino]methyl]-2-azabicyclo[2.1.1]hexan-4-yl]methoxy]-1-methylpyridin-2-one was deprotected according to General Method **8** in anhydrous DCM (2 mL) and TFA (1.2 mL, 16.1 mmol) at rt for 16 h. The mixture was concentrated and diluted with NaOH(aq) (4M, 10mL) and extracted with a mixture of $CHCl_3$ and IPA (3:1, 3 x 10 mL). The organic layers were combined, washed with brine (15 mL), dried (Na_2SO_4) and concentrated. The product was purified by automated prep HPLC (mass directed, 32-42% MeCN in water [10 mM NH_4HCO_3]) and lyophilized to afford the product (57 mg, 56% over 2 steps) as a solid.

[M+H]+ = 550.3

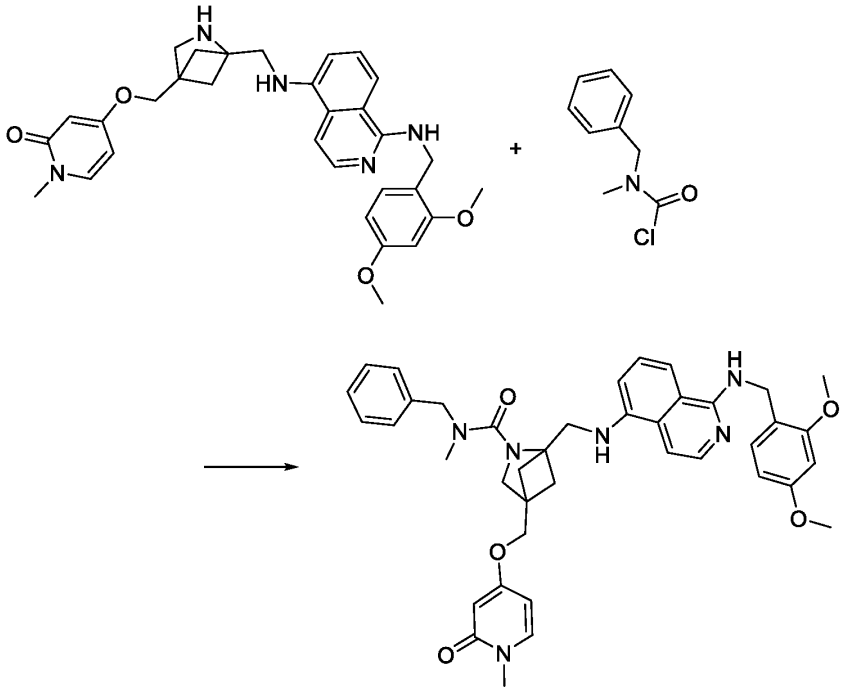
^{1}H NMR (DMSO-d6, 500 MHz) δ 1.50 (2H, d, J = 4.4 Hz), 1.90 (2H, d, J = 4.7 Hz), 3.30 (3H, s), 3.60 (2H, s), 3.74 (2H, s), 3.99 (2H, d, J = 6.5 Hz), 4.13 (2H, s), 5.77 (1H, d, J = 2.8 Hz), 5.87 (1H, dd, J = 7.5, 2.8 Hz), 6.16 (1H, t, J = 6.7 Hz), 6.53 (2H, s), 6.78 (2H, dd, J = 13.3, 7.0 Hz), 6.90 (1H, dd, J = 2.2, 1.0 Hz), 7.19 (1H, t, J = 7.9 Hz), 7.25 (1H, dd, J = 8.4, 1.8 Hz), 7.32 (1H, d, J = 8.3 Hz), 7.50 - 7.55 (2H, m), 7.57 (1H, d, J = 1.8 Hz), 7.67 (1H, d, J = 6.1 Hz), 7.97 (1H, d, J = 2.2 Hz).

Example Number 12041

1-[[(1-Aminoisoquinolin-5-yl)amino]methyl]-N-benzyl-N-methyl-4-[(1-methyl-2-oxopyridin-4-yl)oxymethyl]-2-azabicyclo[2.1.1]hexane-2-carboxamide



N-Benzyl-1-[[[1-[(2,4-dimethoxyphenyl)methylamino]-5-isoquinolyl]amino]methyl]-N-methyl-4-[(1-methyl-2-oxo-4-pyridyl)oxymethyl]-2-azabicyclo[2.1.1]hexane-2-carboxamide

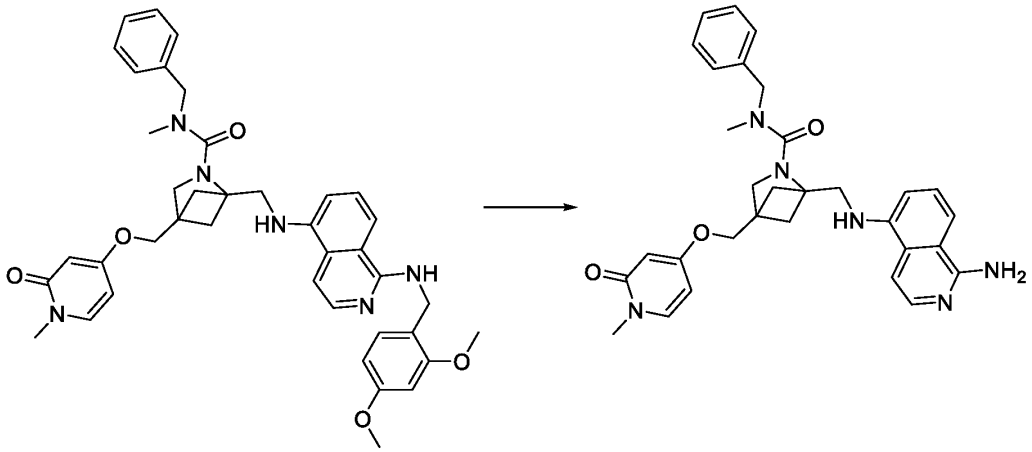


A mixture of N-methyl-1-phenyl-methanamine (1300 µL, 9.77 mmol) and DIPEA (3400 µL, 19.8 mmol) in anhydrous DCM (20 mL) was added over 30 min to a solution of phosgene in toluene (20 wt%, 12 mL, 25.8 mmol) at 0 °C. The mixture was stirred at 0 °C for 3 h and concentrated. The residue was triturated with Et_2O (20 mL). The solid was filtered, washed with Et_2O (3 x 20 mL) and the filtrate was concentrated to afford N-benzyl-N-methyl-carbamoyl chloride (2136 mg). N-Benzyl-N-methyl-carbamoyl chloride (37.2 mg, 0.162 mmol) in anhydrous THF (1 mL) was added to a mixture of 4-[[4-[[[1-[(2,4-dimethoxyphenyl)methylamino]-5-isoquinolyl]amino]methyl]-2-azabicyclo[2.1.1]hexan-1-yl]methoxy]-1-

methyl-pyridin-2-one (79.3 mg, 0.139 mmol) and TEA (50 µL, 0.36 mmol) in THF (1 mL) at rt. The mixture was stirred for 18 h and additional N-benzyl-N methyl-carbamoyl chloride (23 mg, 0.104 mmol) in anhydrous THF (500 µL) was added at rt. The mixture was stirred at rt for 18 h and concentrated to provide the product as a solid.

$[M+H]^+$ = 689.2

1-[[(1-Amino-5-isoquinolyl)amino]methyl]-N-benzyl-N-methyl-4-[(1-methyl-2-oxo-4-pyridyl)oxymethyl]-2-azabicyclo[2.1.1]hexane-2-carboxamide (Example 12041)



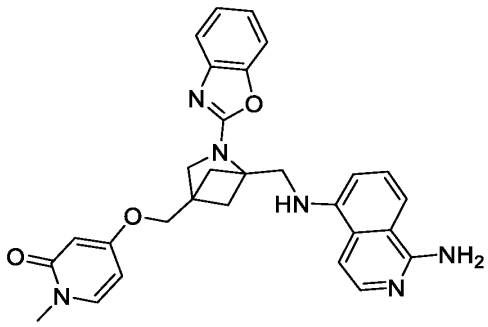
N-Benzyl-1-[[[1-[(2,4-dimethoxyphenyl)methylamino]-5-isoquinolyl]amino]methyl]-N-methyl-4-[(1-methyl-2-oxo-4-pyridyl)oxymethyl]-2-azabicyclo[2.1.1]hexane-2-carboxamide was deprotected according to General Method **8** in DCM (750 µL) and TFA (750 µL, 10.0 mmol) at rt. The mixture was stirred for 3 h and diluted with NaOH(aq) (2M, 10 mL). The mixture was stirred for 10 min and the aq. phase was extracted with a mixture of DCM and MeOH (9:1 v/v, 3 x 20 mL). The combined organic phases were dried (Na_2SO_4), filtered and concentrated. The residue was diluted with a mixture of MeOH and MeCN (1:1 v/v, 2 mL) and loaded onto a PL-HCO_3 MP SPE cartridge (200 mg). The cartridge was washed with a mixture of MeOH and MeCN (1:1 v/v, 3 x 2 mL) and the filtrate was concentrated. The residue was purified by flash chromatography (Silica-C18, 25-50% MeCN in water [10 mM NH_4HCO_3]) and lyophilized to provide the product (42.7 mg, 57% yield over two steps) as a solid.

$[M+H]^+$ = 539.4.

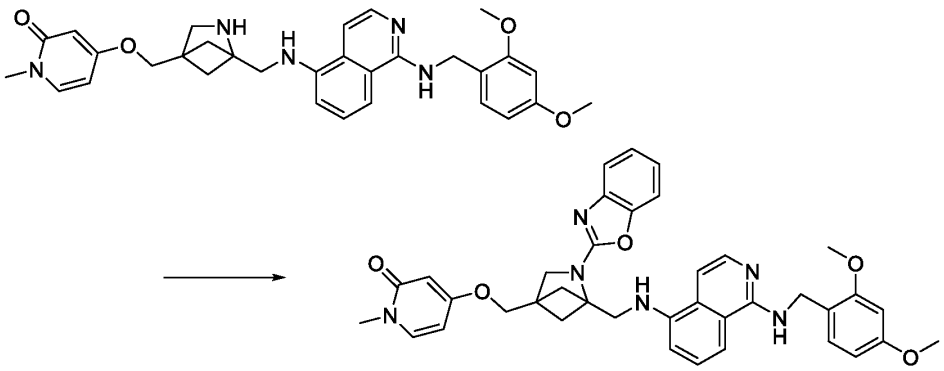
^{1}H NMR (DMSO-d6, 400 MHz) δ 1.57 - 1.64 (2H, m), 1.72 - 1.79 (2H, m), 2.82 (3H, s), 3.30 (3H, s), 3.30 (2H, s), 3.85 (2H, d, J = 6.1 Hz), 4.12 (2H, s), 4.50 (2H, s), 5.74 (1H, d, J = 2.8 Hz), 5.87 (1H, dd, J = 7.5, 2.8 Hz), 6.16 (1H, t, J = 6.2 Hz), 6.47 (2H, s), 6.74 (1H, d, J = 7.8 Hz), 7.06 - 7.11 (1H, m), 7.18 (1H, t, J = 8.0 Hz), 7.23 - 7.39 (6H, m), 7.51 (1H, d, J = 7.5 Hz), 7.71 (1H, d, J = 6.1 Hz).

Example Number 12057

4-((1-(((1-Aminoisoquinolin-5-yl)amino)methyl)-2-(benzo[d]oxazol-2-yl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one



4-[[2-(1,3-Benzoxazol-2-yl)-1-[[[1-[(2,4-dimethoxyphenyl)methylamino]-5-isoquinolyl]amino]methyl]-2-azabicyclo[2.1.1]hexan-4-yl]methoxy]-1-methyl-pyridin-2-one



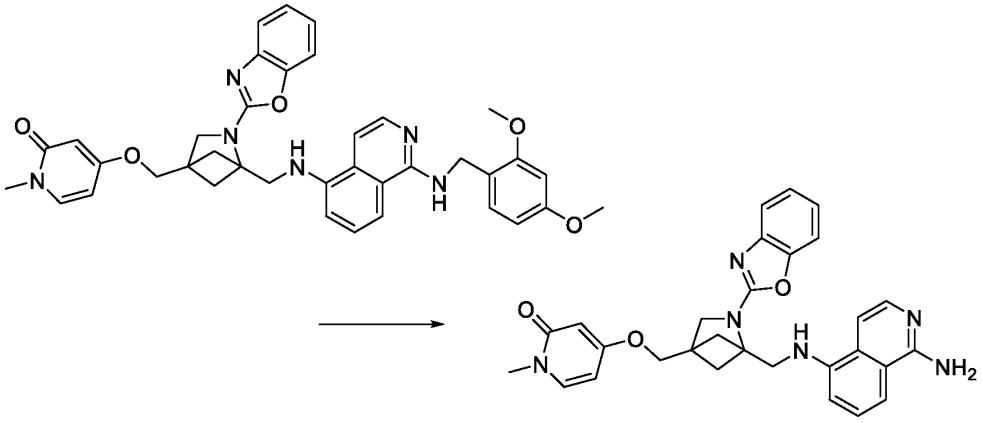
A mixture of 4-[[4-[[[1-[(2,4-dimethoxyphenyl)methylamino]-5-isoquinolyl]amino]methyl]-2-azabicyclo[2.1.1]hexan-1-yl]methoxy]-1-methyl-pyridin-2-one (75 mg, 0.138 mmol), 2-chloro-1,3-benzoxazole (24 mg, 0.156 mmol) and K_2CO_3 (60 mg, 0.434 mmol) in anhydrous DMSO (1 mL) was heated to 140 °C and stirred for 72 h. The mixture was cooled to rt and was quenched with brine (20 mL). The aqueous phase was extracted with EtOAc (3 x 25 mL) and the combined organic layers were washed with brine (2 x 20 mL), dried (Na_2SO_4), filtered and concentrated. Flash chromatography (Silica, 40% MeOH in DCM) afforded the product (66.7 mg, 70% yield).

$[M+H]^+$ = 659.4

^{1}H NMR (DMSO-*d6*, 400 MHz) δ 1.67 (2H, dd, J = 4.7, 1.8 Hz), 1.95 - 1.99 (2H, m), 3.27 (3H, s), 3.66 (5H, s), 3.78 (3H, s), 4.12 - 4.23 (4H, m), 4.54 (2H, d, J = 5.7 Hz), 5.75 (1H, d, J = 2.8 Hz), 5.86 (1H, dd, J = 7.5, 2.8 Hz), 6.34 (1H, dd, J = 8.4, 2.4 Hz), 6.46 - 6.53 (2H, m), 6.80 (1H, d, J = 7.8 Hz), 6.95 - 6.99 (3H, m), 7.02 (1H,

td, J = 7.8, 1.3 Hz), 7.14 (1H, td, J = 7.7, 1.1 Hz), 7.22 (1H, t, J = 8.0 Hz), 7.31 - 7.44 (4H, m), 7.49 (1H, d, J = 7.6 Hz), 7.66 (1H, d, J = 6.1 Hz)

4-((1-(((1-Aminoisoquinolin-5-yl)amino)methyl)-2-(benzo[d]oxazol-2-yl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one (Example 12057)



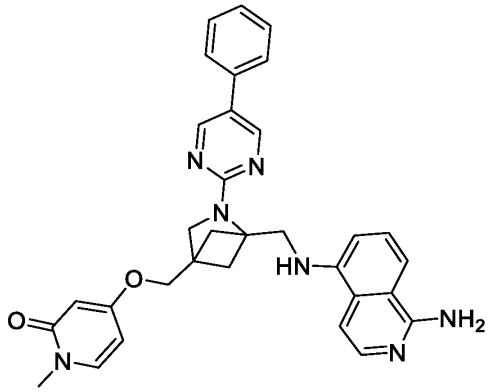
4-[[2-(1,3-Benzoxazol-2-yl)-1-[[[1-[(2,4-dimethoxyphenyl)methylamino]-5-isoquinolyl]amino]methyl]-2-azabicyclo[2.1.1]hexan-4-yl]methoxy]-1-methylpyridin-2-one (66.7 mg, 0.0962 mmol) was deprotected according to General Method **8** in anhydrous DCM (1 mL) and TFA (300 µL, 4.04 mmol) at rt for 18 h. The mixture was quenched with 1M NaOH(aq) (25 mL) and DCM (25 mL). The layers were separated and the aqueous layer was extracted with 1:3 IPA:$CHCl_3$ (2 x 20 mL). The combined organic layers were washed with brine (25 mL), dried (Na_2SO_4), filtered and concentrated. The product was purified by flash chromatography (Silica-C18, 0-75% MeCN in water [10 mM NH_4HCO_3]) and lyophilised to afford the product (27.3 mg, 56% yield).

$[M+H]^+$ = 509.2

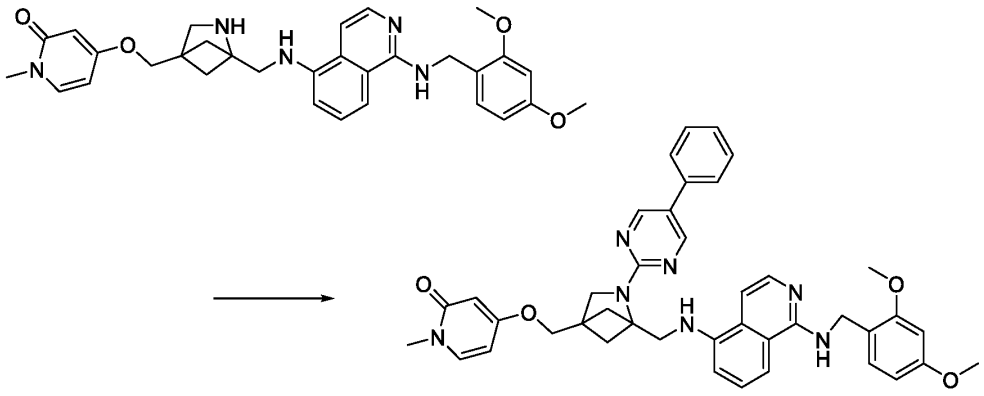
^{1}H NMR (DMSO-d6, 400 MHz) δ 1.67 (2H, dd, J = 4.7, 1.8 Hz), 1.97 (2H, d, J = 4.8 Hz), 3.27 (3H, s), 3.66 (2H, s), 4.11 - 4.21 (4H, m), 5.76 (1H, d, J = 2.8 Hz), 5.86 (1H, dd, J = 7.5, 2.8 Hz), 6.47 (3H, s), 6.77 (1H, d, J = 7.7 Hz), 6.97 - 7.00 (1H, m), 7.02 (1H, td, J = 7.7, 1.3 Hz), 7.13 - 7.17 (1H, m), 7.20 (1H, d, J = 7.9 Hz), 7.30 (1H, d, J = 8.4 Hz), 7.32 - 7.35 (1H, m), 7.39 (1H, ddd, J = 7.9, 1.2, 0.6 Hz), 7.49 (1H, d, J = 7.6 Hz), 7.66 (1H, d, J = 6.0 Hz)

Example Number 12060

4-((1-(((1-Aminoisoquinolin-5-yl)amino)methyl)-2-(5-phenylpyrimidin-2-yl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one



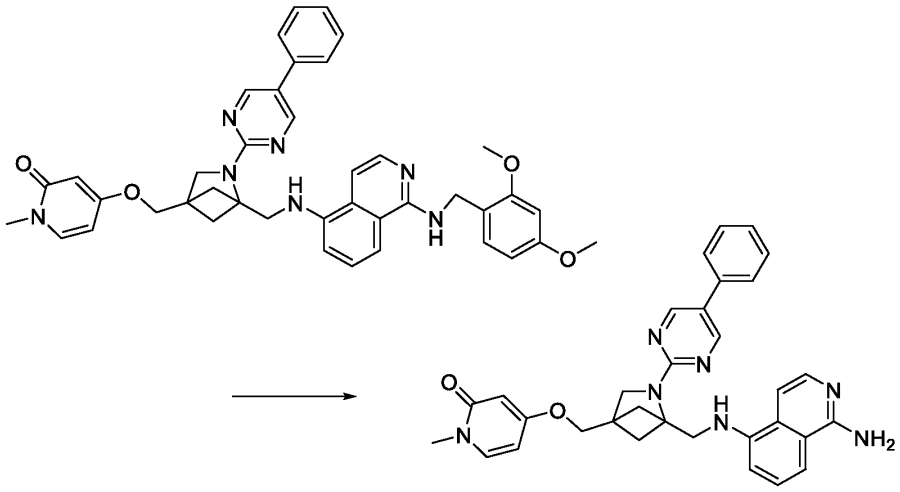
4-[[1-[[[1-[(2,4-Dimethoxyphenyl)methylamino]-5-isoquinolyl]amino]methyl]-2-(5-phenylpyrimidin-2-yl)-2-azabicyclo[2.1.1]hexan-4-yl]methoxy]-1-methyl-pyridin-2-one



DIPEA (23 µL, 0.164 mmol) was added to a mixture of 4-[[4-[[[1-[(2,4-dimethoxyphenyl)methylamino]-5-isoquinolyl]amino]methyl]-2-azabicyclo[2.1.1]hexan-1-yl]methoxy]-1-methyl-pyridin-2-one (60 mg, 0.111 mmol) and 2-chloro-5-phenyl-pyrimidine (22 mg, 0.115 mmol) in DMF (1000 µL) at rt. The mixture was stirred at 100 °C for 48 h then concentrated. The product was purified by flash chromatography (Silica, 0-40% MeOH in EtOAc to afford the product (61 mg, 79% yield).

$[M+H]^+$ = 696.4

4-((1-(((1-Aminoisoquinolin-5-yl)amino)methyl)-2-(5-phenylpyrimidin-2-yl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one (Example 12060)



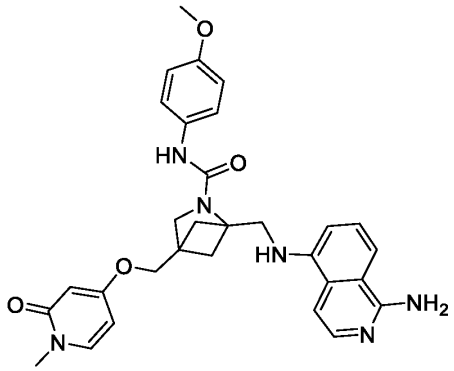
4-[[1-[[[1-[(2,4-Dimethoxyphenyl)methylamino]-5-isoquinolyl]amino]methyl]-2-(5-phenylpyrimidin-2-yl)-2-azabicyclo[2.1.1]hexan-4-yl]methoxy]-1-methyl-pyridin-2-one (61 mg, 0.0877 mmol) was deprotected according to General Method **8** in DCM (1000 µL) and TFA (130 µL, 1.75 mmoL) at rt for 18 h then concentrated. The residue was loaded onto a PL-HCO_3 MP SPE cartridge eluting with a mixture of MeCN and MeOH (1:1 v/v, 3 x 2 mL). The product was purified by flash chromatography (C18, 5-80% MeCN in water [10 mM NH_4HCO_3]) then lyophilized to afford the product (33 mg, 69% yield).

$[M+H]^+$ = 546.3

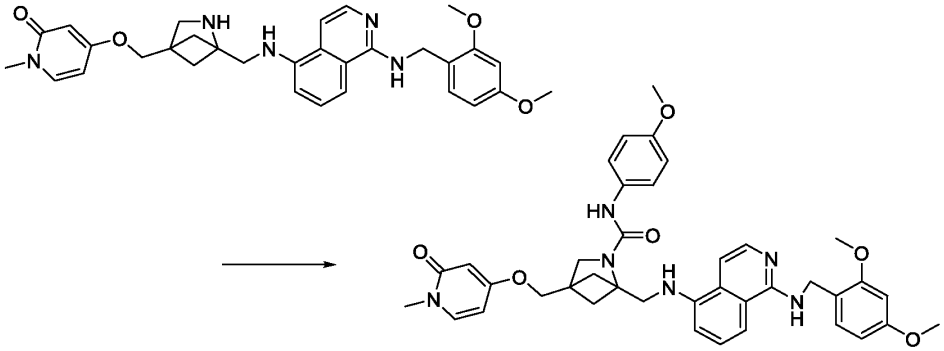
^{1}H NMR (DMSO-d6, 400 MHz) δ 1.68 (2H, d, J = 3.0 Hz), 2.02 (2H, d, J = 4.3 Hz), 3.31 (3H, s), 3.61 (2H, s), 4.22 (2H, s), 4.26 (2H, d, J = 6.4 Hz), 5.81 (1H, d, J = 2.8 Hz), 5.91 (1H, dd, J = 7.5, 2.8 Hz), 6.31 (1H, t, J = 6.4 Hz), 6.50 (2H, s), 6.81 (1H, d, J = 7.7 Hz), 6.96 (1H, d, J = 6.2 Hz), 7.23 (1H, t, J = 8.0 Hz), 7.30 - 7.38 (2H, m), 7.46 (2H, t, J = 7.7 Hz), 7.54 (1H, d, J = 7.6 Hz), 7.64 - 7.73 (3H, m), 8.75 (2H, s)

Example Number 12061

1-(((1-Aminoisoquinolin-5-yl)amino)methyl)-N-(4-methoxyphenyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxamide,



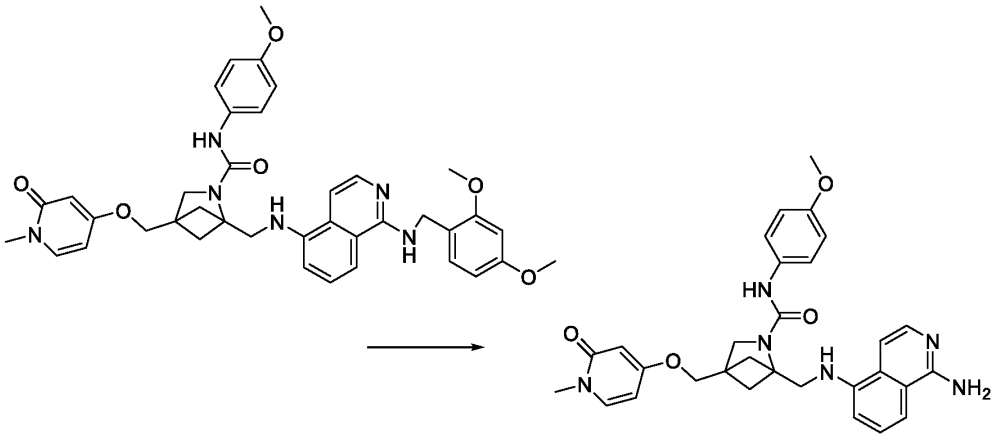
1-[[[1-[(2,4-Dimethoxyphenyl)methylamino]-5-isoquinolyl]amino]methyl]-N-(4-methoxyphenyl)-4-[(1-methyl-2-oxo-4-pyridyl)oxymethyl]-2-azabicyclo[2.1.1]hexane-2-carboxamide



TEA (48 uL, 0.34 mmol) was added to a mixture of 4-[[4-[[[1-[(2,4-dimethoxyphenyl)methylamino]-5-isoquinolyl]amino]methyl]-2-azabicyclo[2.1.1]hexan-1-yl]methoxy]-1-methyl-pyridin-2-one (60 mg, 0.11 mmol) and 1-(isocyanatomethyl)-4-methoxy-benzene (17 uL, 0.12 mmol) in THF (1 mL) at rt. The mixture was stirred at rt for 30 min then concentrated to afford the product (101 mg).

$[M+H]^+ = 691.4$

1-(((1-Aminoisoquinolin-5-yl)amino)methyl)-N-(4-methoxyphenyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxamide (Example 12061)



1-[[[1-[(2,4-Dimethoxyphenyl)methylamino]-5-isoquinolyl]amino]methyl]-N-(4-methoxyphenyl)-4-[(1-methyl-2-oxo-4-pyridyl)oxymethyl]-2-azabicyclo[2.1.1]hexane-2-carboxamide (101 mg) was deprotected according to General Method **8** in DCM (1.0 mL) and TFA (165 µL, 2.22 mL) at rt for 18 h then

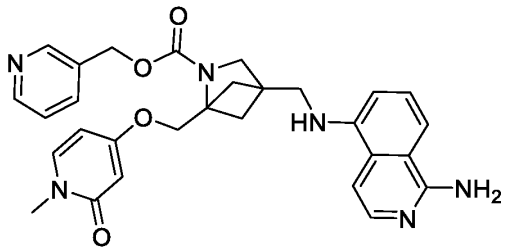
concentrated. The material was loaded onto a PL-HCO_3 MP SPE cartridge eluting with a mixture of MeCN and MeOH (1:1 v/v, 3 x 2 mL). The crude product was purified by flash chromatography (C18, 5-65% MeCN in water [10 mM NH_4HCO_3 then lyophilized to afford the product (36 mg, 60% yield).

$[M+H]^+$ = 541.3

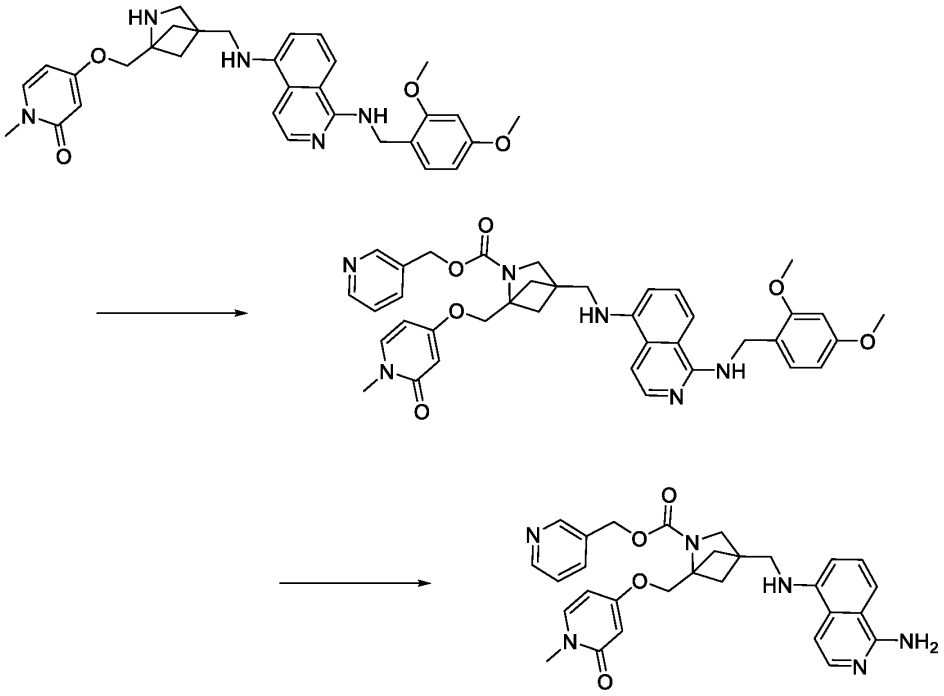
^{1}H NMR (DMSO-d6, 400 MHz) δ 1.57 (2H, d, J = 3.0 Hz), 1.85 (2H, d, J = 4.2 Hz), 3.31 (3H, s), 3.50 (2H, s), 3.71 (3H, s), 3.99 (2H, d, J = 6.1 Hz), 4.17 (2H, s), 5.78 (1H, d, J = 2.8 Hz), 5.89 (1H, dd, J = 7.5, 2.8 Hz), 6.23 (1H, t, J = 6.5 Hz), 6.49 (2H, s), 6.75 (1H, d, J = 7.6 Hz), 6.80 - 6.88 (2H, m), 6.97 (1H, d, J = 6.0 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.32 (1H, d, J = 8.3 Hz), 7.37 - 7.45 (2H, m), 7.53 (1H, d, J = 7.6 Hz), 7.71 (1H, d, J = 6.1 Hz), 8.35 (1H, s)

Example Number 13009

Pyridin-3-ylmethyl4-(((1-aminoisoquinolin-5-yl)amino)methyl)-1-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate,



Pyridin-3-ylmethyl4-(((1-aminoisoquinolin-5-yl)amino)methyl)-1-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate (Example 13009)



CDI (65 mg, 0.381 mmol) was added to a mixture of 3-pyridylmethanol (45.3 mg, 0.407 mmol) in MeCN (1 mL). The mixture was stirred at rt for 1 h and a solution of 4-((4-(((1-((2,4-dimethoxybenzyl)amino)isoquinolin-5-yl)amino)methyl)-2-azabicyclo[2.1.1]hexan-1-yl)methoxy)-1-methylpyridin-2(1H)-one (81.8 mg, 0.151 mmol) and DBU (10 µL, 0.0775 mmol) in MeCN (1 mL) was added at rt. The mixture was stirred at rt for 18 h and concentrated. The intermediate 3-pyridylmethyl 4-[[[1-[(2,4-dimethoxyphenyl)methylamino]-5-isoquinolyl]amino]methyl]-1-[(1-methyl-2-oxo-4-pyridyl)oxymethyl]-2-azabicyclo[2.1.1]hexane-2-carboxylate was deprotected according to General Method **8** in DCM (750 µL) and TFA (750 µL, 10.0 mmol) at rt for 6 h. 2M NaOH(aq) (10 mL) was added and the mixture was stirred for 10 min. The aq phase was extracted with a mixture of DCM and MeOH (9:1 v/v, 3 x 20 mL). The combined organic phases were dried (Na_2SO_4), filtered and concentrated. The residue was diluted with a mixture of MeOH and MeCN (1:1 v/v, 2 mL) and loaded onto a PL-HCO_3 MP SPE cartridge (250 mg). The cartridge was washed with a mixture of MeOH and MeCN (1:1 v/v, 3 x 2 mL) and the filtrate was concentrated. The residue was purified by flash chromatography (Silica-C18, 25-38% MeCN in water [10 mM NH_4HCO_3]) and lyophilized to provide the product (50.2 mg, 63% yield over two steps).

$[M+H]^+$ = 527.3.

^{1}H NMR (DMSO-d6, 400 MHz) δ 1.53 - 1.61 (2H, m), 1.83 - 1.90 (2H, m), 3.26 (3H, s), 3.40 (2H, s), 3.47 (2H, d, J = 5.8 Hz), 4.42 (2H, s), 5.00 (2H, s), 5.60 (1H, s), 5.80 (1H, d, J = 7.5 Hz), 5.94 (1H, t, J = 6.0 Hz), 6.43

(2H, s), 6.63 (1H, d, J = 7.6 Hz), 7.11 (1H, dd, J = 6.4, 0.8 Hz), 7.15 (1H, t, J = 8.0 Hz), 7.24 - 7.34 (2H, m), 7.45 (1H, d, J = 7.6 Hz), 7.64 - 7.72 (2H, m), 8.45 (1H, d, J = 4.8 Hz), 8.49 (1H, s).

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EXAMPLES

Table 14: Compound Names

Example No	Name
1001	N5-((3-((imidazo[1,2-a]pyridin-7-yloxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine
1002	N5-((3-(((5,6,7,8-tetrahydroimidazo[1,2-a]pyridin-7-yl)oxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine
1002.1	(S*)-N5-((3-(((5,6,7,8-Tetrahydroimidazo[1,2-a]pyridin-7-yl)oxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine
1002.2	(R*)-N5-((3-(((5,6,7,8-tetrahydroimidazo[1,2-a]pyridin-7-yl)oxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine
1003	N5-((3-(((1-methylpiperidin-4-yl)oxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine
1004	N5-((3-((5,6-dihydroimidazo[1,2-a]pyrazin-7(8H)-yl)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine
1005	N5-((3-((5-isopropyl-2,5-diazabicyclo[2.2.1]heptan-2-yl)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine
1005.1	N5-((3-(((1S,4S)-5-isopropyl-2,5-diazabicyclo[2.2.1]heptan-2-yl)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine
1005.2	N5-((3-(((1R,4R)-5-isopropyl-2,5-diazabicyclo[2.2.1]heptan-2-yl)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine
1006	N5-((3-(((2-methylimidazo[1,2-a]pyridin-7-yl)oxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine
1007	N5-((3-(((8-methylimidazo[1,2-a]pyridin-7-yl)oxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine
1008	4-chloro-N6-((3-((imidazo[1,2-a]pyridin-7-yloxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,6-diamine
1009	N-((3-((imidazo[1,2-a]pyridin-7-yloxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)-1H-pyrrolo[2,3-b]pyridin-4-amine
1010	3-chloro-N-((3-((imidazo[1,2-a]pyridin-7-yloxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)-1H-pyrrolo[2,3-b]pyridin-5-amine

Example No	Name
1011	N-((3-((imidazo[1,2-a]pyridin-7-yloxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinolin-6-amine
1012	N-((3-((imidazo[1,2-a]pyridin-7-yloxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)-2-methyl-1H-pyrrolo[2,3-b]pyridin-4-amine
1013	5-[[3-(imidazo[1,2-a]pyridin-7-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methoxy]isoquinolin-1-amine
1014	5-[2-[3-imidazo[1,2-a]pyridin-7-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]ethyl]isoquinolin-1-amine
1015	[3-[(1-aminoisoquinolin-5-yl)oxymethyl]-1-bicyclo[1.1.1]pentanyl]-(6,8-dihydro-5H-imidazo[1,2-a]pyrazin-7-yl)methanone
1016	[3-[[(1-aminoisoquinolin-5-yl)amino]methyl]-1-bicyclo[1.1.1]pentanyl]-(6,8-dihydro-5H-imidazo[1,2-a]pyrazin-7-yl)methanone
1017	5-N-[[3-(imidazo[1,2-a]pyridin-6-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methyl]isoquinoline-1,5-diamine
1018	5-N-[[3-(imidazo[1,2-a]pyridin-8-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methyl]isoquinoline-1,5-diamine
1019	4-[[3-[[(1-aminoisoquinolin-5-yl)amino]methyl]-1-bicyclo[1.1.1]pentanyl]methoxy]-1-methylpyridin-2-one
1101	5-N-[[3-(1H-pyrrolo[3,2-b]pyridin-6-yloxymethyl)-1-bicyclo[1.1.1]pentanyl]methyl]isoquinoline-1,5-diamine
1104	7-((3-(((1-aminoisoquinolin-5-yl)amino)methyl)bicyclo[1.1.1]pentan-1-yl)methoxy)quinazolin-4(1H)-one
1105	N5-((3-(((1H-benzo[d]imidazol-6-yl)oxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine
1106	N5-((3-(((5,6,7,8-tetrahydroimidazo[1,2-a]pyridin-6-yl)oxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine
1108	N5-((3-(((3-(difluoromethyl)-[1,2,4]triazolo[4,3-b]pyridazin-6-yl)oxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine
1109	6-((3-(((1-aminoisoquinolin-5-yl)amino)methyl)bicyclo[1.1.1]pentan-1-yl)methoxy)isoindolin-1-one
1110	N5-((3-(([1,2,4]triazolo[1,5-a]pyridin-7-yloxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine

Example No	Name
1112	7-((3-(((1-aminoisoquinolin-5-yl)amino)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)-7,8-dihydroimidazo[1,2-a]pyrazin-6(5H)-one
1113	6-((3-(((1-aminoisoquinolin-5-yl)amino)methyl)bicyclo[1.1.1]pentan-1-yl)methoxy)indolin-2-one
1114	N5-((3-(((octahydroindolizin-7-yl)oxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine
1115	N5-((3-(((5-chloroimidazo[1,2-a]pyridin-7-yl)oxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine
1116	N5-((3-(((5-fluoroimidazo[1,2-a]pyridin-7-yl)oxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine
1117	N5-((3-(((5-methylimidazo[1,2-a]pyridin-7-yl)oxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine
1118	N5-((3-(((6,7-dihydro-5H-pyrrolo[1,2-a]imidazol-6-yl)oxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine
1119	N5-((3-(imidazo[1,2-a]pyridin-7-ylmethoxy)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine
1120	4-((3-((1-aminoisoquinolin-5-yl)amino)bicyclo[1.1.1]pentan-1-yl)methoxy)-1-methylpyridin-2(1H)-one
1121	N5-(3-((imidazo[1,2-a]pyridin-7-yloxy)methyl)bicyclo[1.1.1]pentan-1-yl)isoquinoline-1,5-diamine
1122	N5-(3-(((5,6,7,8-tetrahydroimidazo[1,2-a]pyridin-7-yl)oxy)methyl)bicyclo[1.1.1]pentan-1-yl)isoquinoline-1,5-diamine
1123	N5-(3-(imidazo[1,2-a]pyridin-7-ylmethoxy)bicyclo[1.1.1]pentan-1-yl)isoquinoline-1,5-diamine
1124	N5-(3-((5,6,7,8-tetrahydroimidazo[1,2-a]pyridin-7-yl)methoxy)bicyclo[1.1.1]pentan-1-yl)isoquinoline-1,5-diamine
1125	N5-((3-(((1H-indazol-6-yl)oxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine
1126	N5-((3-(imidazo[1,2-a]pyridin-1(8aH)-ylmethyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine
1127	1-((3-(((1-aminoisoquinolin-5-yl)amino)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)imidazo[1,2-a]pyridin-7(1H)-one

Example No	Name
1129	3-chloro-N-((3-((imidazo[1,2-a]pyridin-7-yloxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)-1H-pyrrolo[2,3-b]pyridin-5-amine
1130	2-chloro-N-((3-(((5,6,7,8-tetrahydroimidazo[1,2-a]pyridin-7-yl)oxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)-1H-pyrrolo[2,3-b]pyridin-4-amine
1131	N5-(3-((imidazo[1,2-a]pyridin-6-yloxy)methyl)bicyclo[1.1.1]pentan-1-yl)isoquinoline-1,5-diamine
1132	N-(3-(((1-aminoisoquinolin-5-yl)amino)methyl)bicyclo[1.1.1]pentan-1-yl)-3-(difluoromethyl)-[1,2,4]triazolo[4,3-a]pyridine-6-carboxamide
1133	5-((3-(((1-aminoisoquinolin-5-yl)amino)methyl)bicyclo[1.1.1]pentan-1-yl)methoxy)isoindolin-1-one
1134	4-((3-(((1-aminoisoquinolin-5-yl)amino)methyl)bicyclo[1.1.1]pentan-1-yl)methoxy)-1,6-dimethylpyridin-2(1H)-one
1135	N5-((3-(([1,2,4]triazolo[4,3-a]pyridin-7-yloxy)methyl)bicyclo[1.1.1]pentan-1-yl)methyl)isoquinoline-1,5-diamine
2020	5-N-[[1-(imidazo[1,2-a]pyridin-7-yloxymethyl)-2-oxabicyclo[2.1.1]hexan-4-yl]methyl]isoquinoline-1,5-diamine
2021	N-((1-((imidazo[1,2-a]pyridin-7-yloxy)methyl)-2-oxabicyclo[2.1.1]hexan-4-yl)methyl)-2-methyl-1H-pyrrolo[2,3-b]pyridin-4-amine
2022	5-N-[[1-(imidazo[1,2-a]pyridin-6-yloxymethyl)-2-oxabicyclo[2.1.1]hexan-4-yl]methyl]isoquinoline-1,5-diamine
2201	5-((1-((imidazo[1,2-a]pyridin-7-yloxy)methyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)isoquinolin-1-amine
2202	1-(4-(((1-aminoisoquinolin-5-yl)oxy)methyl)-1-((imidazo[1,2-a]pyridin-7-yloxy)methyl)-2-azabicyclo[2.1.1]hexan-2-yl)ethan-1-one
2203	5-((4-((imidazo[1,2-a]pyridin-7-yloxy)methyl)bicyclo[2.1.1]hexan-1-yl)methoxy)isoquinolin-1-amine
2204	N5-((1-(((3-(difluoromethyl)-[1,2,4]triazolo[4,3-b]pyridazin-6-yl)oxy)methyl)-2-oxabicyclo[2.1.1]hexan-4-yl)methyl)isoquinoline-1,5-diamine
2205	4-((4-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methoxy)-1-methylpyridin-2(1H)-one

Example No	Name
2206	N5-((1-(((3-(trifluoromethyl)-[1,2,4]triazolo[4,3-a]pyridin-7-yl)oxy)methyl)-2-oxabicyclo[2.1.1]hexan-4-yl)methyl)isoquinoline-1,5-diamine
2207	N5-((1-(([1,2,4]triazolo[1,5-a]pyridin-7-yloxy)methyl)-2-oxabicyclo[2.1.1]hexan-4-yl)methyl)isoquinoline-1,5-diamine
2208	2-((4-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methoxy)pyrimidine-5-carbonitrile
2210	N5-((1-(([1,2,4]triazolo[1,5-a]pyridin-6-yloxy)methyl)-2-oxabicyclo[2.1.1]hexan-4-yl)methyl)isoquinoline-1,5-diamine
2211	6-((4-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methoxy)-2-methylisoindolin-1-one
2212	N5-((1-(((3-methylimidazo[1,2-a]pyridin-6-yl)oxy)methyl)-2-oxabicyclo[2.1.1]hexan-4-yl)methyl)isoquinoline-1,5-diamine
3023	N5-((1-((imidazo[1,2-a]pyridin-7-yloxy)methyl)-3,3-dimethyl-2-oxabicyclo[2.1.1]hexan-4-yl)methyl)isoquinoline-1,5-diamine
3024	5-((1-((imidazo[1,2-a]pyridin-7-yloxy)methyl)-3,3-dimethyl-2-oxabicyclo[2.1.1]hexan-4-yl)methoxy)isoquinolin-1-amine
4401	N5-((trans-3-((imidazo[1,2-a]pyridin-7-yloxy)methyl)cyclobutyl)methyl)isoquinoline-1,5-diamine
4402	N5-((trans-3-(imidazo[1,2-a]pyridin-7-ylmethoxy)cyclobutyl)methyl)isoquinoline-1,5-diamine
4403	4-((trans-3-(((1-aminoisoquinolin-5-yl)amino)methyl)cyclobutoxy)methyl)-1-methylpyridin-2(1H)-one
5003	N5-((cis-3-((imidazo[1,2-a]pyridin-7-yloxy)methyl)cyclobutyl)methyl)isoquinoline-1,5-diamine
6601	5-N-[[4-(imidazo[1,2-a]pyridin-7-yloxymethyl)-2-oxabicyclo[2.1.1]hexan-1-yl]methyl]isoquinoline-1,5-diamine
6602	N5-((4-((imidazo[1,2-a]pyridin-6-yloxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
6603	5-((4-((imidazo[1,2-a]pyridin-7-yloxy)methyl)-2-azabicyclo[2.1.1]hexan-1-yl)methoxy)isoquinolin-1-amine
6604	1-(1-(((1-aminoisoquinolin-5-yl)oxy)methyl)-4-((imidazo[1,2-a]pyridin-7-yloxy)methyl)-2-azabicyclo[2.1.1]hexan-2-yl)ethan-1-one

Example No	Name
6605	N-((4-((imidazo[1,2-a]pyridin-7-yloxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)-2-methyl-1H-pyrrolo[2,3-b]pyridin-4-amine
6606	2-chloro-N-((4-((imidazo[1,2-a]pyridin-7-yloxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)-1H-pyrrolo[2,3-b]pyridin-4-amine
6607	N-((4-((imidazo[1,2-a]pyridin-7-yloxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)-2-methyl-1H-pyrrolo[2,3-c]pyridin-4-amine
6608	N5-((4-(((3-(difluoromethyl)-[1,2,4]triazolo[4,3-b]pyridazin-6-yl)oxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
6609	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one
6610	N5-((4-(((5,6,7,8-tetrahydroimidazo[1,2-a]pyridin-6-yl)oxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
6611	2-chloro-N-((4-((imidazo[1,2-a]pyridin-6-yloxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)-1H-pyrrolo[2,3-b]pyridin-4-amine
6612	N5-((4-((imidazo[1,2-b]pyridazin-6-yloxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
6613	N5-((4-(((2-(difluoromethyl)imidazo[1,2-a]pyridin-7-yl)oxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
6614	N5-((4-((imidazo[1,2-a]pyrimidin-7-yloxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
6615	N5-((4-(((2-(trifluoromethyl)imidazo[1,2-b]pyridazin-6-yl)oxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
6616	N5-((4-((imidazo[1,2-a]pyrazin-6-yloxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
6617	N5-((4-(((8-methylimidazo[1,2-a]pyridin-6-yl)oxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
6618	5-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[2.1.1]hexan-4-yl)methoxy)isoindolin-1-one
6619	5-((4-((imidazo[1,2-a]pyridin-6-ylamino)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methoxy)isoquinolin-1-amine
6620	N5-((4-(((3-(difluoromethyl)-[1,2,4]triazolo[4,3-a]pyridin-6-yl)oxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine

Example No	Name
6621	5-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[2.1.1]hexan-4-yl)methoxy)-2-methylisoindolin-1-one
6622	N5-((4-(((7-methylimidazo[1,2-a]pyridin-6-yl)oxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
6623	N5-((4-((imidazo[1,2-c]pyrimidin-7-yloxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
6624	N5-((4-(((3-methylimidazo[1,2-a]pyridin-6-yl)oxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
6625	N5-((4-(((3-fluoroimidazo[1,2-a]pyridin-6-yl)oxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
6626	N5-((4-(((5-methylimidazo[1,2-a]pyridin-6-yl)oxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
6627	N5-((4-(((3-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl)oxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
6628	6-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[2.1.1]hexan-4-yl)methoxy)-2-methylisoindolin-1-one
6629	N5-((4-(([1,2,4]triazolo[4,3-a]pyridin-7-yloxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
6630	N5-((4-(((8-(trifluoromethyl)imidazo[1,2-a]pyridin-6-yl)oxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
6631	N5-((4-(((8-methoxyimidazo[1,2-a]pyridin-6-yl)oxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
6633	N5-((4-(((2-methylimidazo[1,2-a]pyridin-6-yl)oxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
6634	N5-((4-(([1,2,4]triazolo[4,3-a]pyridin-6-yloxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
6635	2-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[2.1.1]hexan-4-yl)methyl)-5-hydroxyisoindoline-1,3-dione
6636	5-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[2.1.1]hexan-4-yl)methoxy)isoindoline-1,3-dione
6637	6-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[2.1.1]hexan-4-yl)methoxy)-3,4-dihydroisoquinolin-1(2H)-one

Example No	Name
6638	N5-((4-(([1,2,4]triazolo[4,3-b]pyridazin-6-yloxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
6639	N5-((4-(((3-cyclopropylimidazo[1,2-a]pyridin-6-yl)oxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
6640	6-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[2.1.1]hexan-4-yl)methoxy)-2-methyl-3,4-dihydroisoquinolin-1(2H)-one
6641	N5-((4-(((8-isopropylimidazo[1,2-a]pyridin-6-yl)oxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
6642	6-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[2.1.1]hexan-4-yl)methoxy)isoindolin-1-one
6643	6-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[2.1.1]hexan-4-yl)methoxy)-2-methylisoquinolin-1(2H)-one
6644	N5-((4-(((3-(difluoromethyl)imidazo[1,2-a]pyridin-6-yl)oxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
6645	N5-((4-((1H-pyrazol-1-yl)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
6646	N5-((4-((1H-imidazol-1-yl)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
6647	N5-((4-((2H-1,2,3-triazol-2-yl)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
6648	N5-((4-((1H-1,2,3-triazol-1-yl)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
6649	1-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[2.1.1]hexan-4-yl)methyl)pyrrolidin-2-one
6650	5-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[2.1.1]hexan-4-yl)methoxy)-3,3-dimethylisoindolin-1-one
6651	5-((1-(((2-chloro-1H-pyrrolo[2,3-b]pyridin-4-yl)amino)methyl)-2-oxabicyclo[2.1.1]hexan-4-yl)methoxy)isoindolin-1-one
6653	1-(3-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[2.1.1]hexan-4-yl)methoxy)phenyl)pyrrolidin-2-one
6654	1-(2-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[2.1.1]hexan-4-yl)methoxy)phenyl)pyrrolidin-2-one

Example No	Name
6656	1,3-dimethyl-N-((4-(((3-methylimidazo[1,2-a]pyridin-6-yl)oxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)-1H-indol-6-amine
6658	2-(((4-(((3-methylimidazo[1,2-a]pyridin-6-yl)oxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)amino)benzonitrile
6659	N-((4-(((3-methylimidazo[1,2-a]pyridin-6-yl)oxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)-2-(2,2,2-trifluoroethyl)aniline
6660	N4-((4-(((3-methylimidazo[1,2-a]pyridin-6-yl)oxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)pyridine-2,4-diamine
6661	N-((4-(((3-methylimidazo[1,2-a]pyridin-6-yl)oxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)pyridin-3-amine
6663	4-methoxy-N-((4-(((3-methylimidazo[1,2-a]pyridin-6-yl)oxy)methyl)-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)pyridin-2-amine
7701	N5-((4-((imidazo[1,2-a]pyridin-7-yloxy)methyl)-3,3-dimethyl-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
7702	5-((4-((imidazo[1,2-a]pyridin-7-yloxy)methyl)-3,3-dimethyl-2-oxabicyclo[2.1.1]hexan-1-yl)methoxy)isoquinolin-1-amine
7703	N5-((4-((imidazo[1,2-a]pyridin-6-yloxy)methyl)-3,3-dimethyl-2-oxabicyclo[2.1.1]hexan-1-yl)methyl)isoquinoline-1,5-diamine
7704	5-((4-((imidazo[1,2-a]pyridin-6-yloxy)methyl)-3,3-dimethyl-2-oxabicyclo[2.1.1]hexan-1-yl)methoxy)isoquinolin-1-amine
8801	5-(6-(imidazo[1,2-a]pyridin-7-ylmethoxy)-2-azaspiro[3.3]heptan-2-yl)isoquinolin-1-amine
8802	6-(6-(imidazo[1,2-a]pyridin-7-ylmethoxy)-2-azaspiro[3.3]heptan-2-yl)isoquinoline
8803	5-(2-(imidazo[1,2-a]pyridin-7-ylmethoxy)-6-azaspiro[3.4]octan-6-yl)isoquinolin-1-amine
8804	5-(cis*-2-(imidazo[1,2-a]pyridin-7-ylmethoxy)-6-azaspiro[3.4]octan-6-yl)isoquinolin-1-amine
8805	5-(trans*-2-(imidazo[1,2-a]pyridin-7-ylmethoxy)-6-azaspiro[3.4]octan-6-yl)isoquinolin-1-amine
8806	5-(trans*-2-((imidazo[1,2-a]pyridin-7-yloxy)methyl)-6-azaspiro[3.4]octan-6-yl)isoquinolin-1-amine

Example No	Name
8807	5-(cis*-2-((imidazo[1,2-a]pyridin-7-yloxy)methyl)-6-azaspiro[3.4]octan-6-yl)isoquinolin-1-amine
8808	5-(6-((imidazo[1,2-a]pyridin-6-yloxy)methyl)-2-azaspiro[3.3]heptan-2-yl)isoquinolin-1-amine
9001	5-(5-(imidazo[1,2-a]pyridin-7-ylmethoxy)-2-azaspiro[3.3]heptan-2-yl)isoquinolin-1-amine
9002	(R*)-5-(5-(imidazo[1,2-a]pyridin-7-ylmethoxy)-2-azaspiro[3.3]heptan-2-yl)isoquinolin-1-amine
9003	(S*)-5-(5-(imidazo[1,2-a]pyridin-7-ylmethoxy)-2-azaspiro[3.3]heptan-2-yl)isoquinolin-1-amine
10901	N5-((5-((imidazo[1,2-a]pyridin-7-yloxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10902	N5-((5-((imidazo[1,2-a]pyridin-7-yloxy)methyl)bicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10903	N5-((5-(((5,6,7,8-tetrahydroimidazo[1,2-a]pyridin-7-yl)oxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10904	N5-((5-((imidazo[1,2-a]pyridin-6-yloxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10906	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[3.1.1]heptan-5-yl)methoxy)-1-methylpyridin-2(1H)-one
10907	N-((5-((imidazo[1,2-a]pyridin-7-yloxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)-2-methyl-1H-pyrrolo[2,3-b]pyridin-4-amine
10908	N5-((5-(((5,6,7,8-tetrahydroimidazo[1,2-a]pyridin-6-yl)oxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10909	2-chloro-N-((5-((imidazo[1,2-a]pyridin-6-yloxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)-1H-pyrrolo[2,3-b]pyridin-4-amine
10910	N5-((5-(((3-(difluoromethyl)-[1,2,4]triazolo[4,3-b]pyridazin-6-yl)oxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10911	3-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[3.1.1]heptan-5-yl)methoxy)-1-methylpyridin-2(1H)-one
10912	N5-((5-((pyrimidin-2-yloxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine

Example No	Name
10914	N5-((5-((pyridin-2-yloxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10915	1-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[3.1.1]heptan-5-yl)methyl)pyridin-2(1H)-one
10918	4-chloro-N-((5-((imidazo[1,2-a]pyridin-7-yloxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)aniline
10919	3-chloro-N-((5-((imidazo[1,2-a]pyridin-7-yloxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)aniline
10920	N5-((5-(((6-methylimidazo[1,2-a]pyridin-7-yl)oxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10921	7-chloro-N-((5-((imidazo[1,2-a]pyridin-7-yloxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)quinolin-4-amine
10922	4-chloro-N6-((5-((imidazo[1,2-a]pyridin-7-yloxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,6-diamine
10923	N5-((5-(((8-methylimidazo[1,2-a]pyridin-7-yl)oxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10924	N5-((5-(((8-chloroimidazo[1,2-a]pyridin-6-yl)oxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10925	N5-((5-(((5-methylimidazo[1,2-a]pyridin-7-yl)oxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10926	N5-((5-(([1,2,4]triazolo[4,3-a]pyridin-7-yloxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10928	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[3.1.1]heptan-5-yl)methoxy)-1,6-dimethylpyridin-2(1H)-one
10929	N5-((5-(([1,2,4]triazolo[4,3-a]pyridin-6-yloxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10930	N5-((5-(((3-methylimidazo[1,2-a]pyridin-7-yl)oxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10931	5-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[3.1.1]heptan-5-yl)methoxy)isoindolin-1-one
10932	N5-((5-(((3-(trifluoromethyl)imidazo[1,2-a]pyridin-7-yl)oxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine

Example No	Name
10933	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[3.1.1]heptan-5-yl)methoxy)-5-chloro-1-methylpyridin-2(1H)-one
10934	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[3.1.1]heptan-5-yl)methoxy)-1-isopropylpyridin-2(1H)-one
10936	N5-((5-((isoxazol-3-yloxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10937	N5-((5-((pyrimidin-4-yloxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10938	6-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[3.1.1]heptan-5-yl)methoxy)-3,4-dihydroisoquinolin-1(2H)-one
10939	6-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[3.1.1]heptan-5-yl)methoxy)-2-methyl-3,4-dihydroisoquinolin-1(2H)-one
10940	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[3.1.1]heptan-5-yl)methoxy)-1-methylpyrimidin-2(1H)-one
10941	6-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[3.1.1]heptan-5-yl)methoxy)isoindolin-1-one
10942	N5-((5-((imidazo[1,2-a]pyridin-6-yloxy)methyl)bicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10943	5-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[3.1.1]heptan-5-yl)methoxy)-1-methylpyridin-2(1H)-one
10944	N5-((5-(((2-methoxypyridin-4-yl)oxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10945	6-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[3.1.1]heptan-5-yl)methoxy)-1-methylpyridin-2(1H)-one
10946	N5-((5-(((1-methyl-1H-1,2,3-triazol-5-yl)oxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10948	N5-((5-(((6-isopropylpyrimidin-4-yl)oxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10949	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[3.1.1]heptan-5-yl)methoxy)-6-isopropyl-1-methylpyridin-2(1H)-one
10951	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[3.1.1]heptan-5-yl)methoxy)-1-methyl-6-(trifluoromethyl)pyridin-2(1H)-one

Example No	Name
10952	1-(((1-aminoisoquinolin-5-yl)amino)methyl)-N-(4-methoxybenzyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxamide
10953	N5-((5-(((2-methylpyridin-4-yl)oxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10954	N5-((5-(((4-methoxypyridin-3-yl)oxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10955	N5-((5-(((4-methylpyridin-2-yl)oxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10956	N5-((5-(((5-methylpyridin-2-yl)oxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10957	N5-((5-(((6-methylpyridin-2-yl)oxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10958	N-((5-((imidazo[1,2-a]pyridin-7-yloxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinolin-6-amine
10961	N5-((5-(((3-(trifluoromethyl)-[1,2,4]triazolo[4,3-a]pyridin-7-yl)oxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10962	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[3.1.1]heptan-5-yl)methoxy)-1,5-dimethylpyrimidin-2(1H)-one
10963	N5-((5-((pyridazin-4-yloxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10964	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[3.1.1]heptan-5-yl)methoxy)-1-ethyl-6-methylpyridin-2(1H)-one
10965	1-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[3.1.1]heptan-5-yl)methyl)pyridazin-4(1H)-one
10966	3-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[3.1.1]heptan-5-yl)methyl)pyridazin-4-ol
10968	N5-((5-((pyridin-3-yloxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10969	N5-((5-(([1,2,3]triazolo[1,5-a]pyridin-5-yloxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine

Example No	Name
10970	3-chloro-N-((5-((imidazo[1,2-a]pyridin-7-yloxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)-1H-indol-5-amine
10971	N5-((5-(((6-methylpyrimidin-4-yl)oxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10972	7-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[3.1.1]heptan-5-yl)methoxy)-2,3-dihydroindolizin-5(1H)-one
10973	N5-((5-((benzo[d]oxazol-6-yloxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10974	N5-((5-(((2-methylpyrimidin-4-yl)oxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
10975	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[3.1.1]heptan-5-yl)methoxy)-1-(difluoromethyl)pyridin-2(1H)-one
10976	N5-((5-((pyrazin-2-yloxy)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methyl)isoquinoline-1,5-diamine
11001	4-((5-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-oxabicyclo[3.1.1]heptan-1-yl)methoxy)-1-methylpyridin-2(1H)-one
12001	benzyl 1-(((1-aminoisoquinolin-5-yl)amino)methyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate
12007	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one
12008	phenyl 1-(((1-aminoisoquinolin-5-yl)amino)methyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate
12009	4-((2-acetyl-1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one
12010	benzyl 1-(((1-aminoisoquinolin-6-yl)amino)methyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate
12011	4-((1-(((1-aminoisoquinolin-6-yl)amino)methyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one
12012	benzyl 1-(((1-aminoisoquinolin-5-yl)amino)methyl)-4-(((2-methyl-3-oxoisoindolin-5-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate
12013	methyl 1-(((1-aminoisoquinolin-6-yl)amino)methyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate

Example No	Name
12014	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(phenethylsulfonyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one
12015	2-chlorophenyl 1-(((1-aminoisoquinolin-5-yl)amino)methyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate
12016	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(3-phenylpropanoyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one
12017	1-(((1-aminoisoquinolin-5-yl)amino)methyl)-N-benzyl-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxamide
12018	benzyl 1-(((1-aminoisoquinolin-5-yl)amino)methyl)-4-(((2-methyl-1-oxoisoindolin-5-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate
12019	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(3-phenylpropyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one
12020	3,4-difluorobenzyl 1-(((1-aminoisoquinolin-5-yl)amino)methyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate
12021	pyridin-2-ylmethyl 1-(((1-aminoisoquinolin-5-yl)amino)methyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate
12022	pyridin-3-ylmethyl 1-(((1-aminoisoquinolin-5-yl)amino)methyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate
12023	2-chlorobenzyl 1-(((1-aminoisoquinolin-5-yl)amino)methyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate
12024	naphthalen-2-ylmethyl 1-(((1-aminoisoquinolin-5-yl)amino)methyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate
12025	benzyl 1-(((2-chloro-1H-pyrrolo[2,3-b]pyridin-4-yl)amino)methyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate
12026	(1-methyl-1H-pyrazol-4-yl)methyl 1-(((1-aminoisoquinolin-5-yl)amino)methyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate
12027	tert-butyl 1-(((1-aminoisoquinolin-5-yl)amino)methyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate
12028	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(2-phenylacetyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one

Example No	Name
12031	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(4-phenylpyrimidin-2-yl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one
12034	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(2-(benzofuran-5-yl)acetyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one
12035	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-benzoyl-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one
12036	1-(((1-aminoisoquinolin-5-yl)amino)methyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-N-phenyl-2-azabicyclo[2.1.1]hexane-2-carboxamide
12038	1-(((1-aminoisoquinolin-5-yl)amino)methyl)-N-benzyl-4-(((1,6-dimethyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxamide
12039	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(2-phenylacetyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1,6-dimethylpyridin-2(1H)-one
12040	4-((2-(2-(1H-indol-4-yl)acetyl)-1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one
12041	1-(((1-aminoisoquinolin-5-yl)amino)methyl)-N-benzyl-N-methyl-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxamide
12042	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(3-(3-methoxyphenyl)propanoyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one
12044	3-(3-(1-(((1-aminoisoquinolin-5-yl)amino)methyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexan-2-yl)-3-oxopropyl)benzonitrile
12045	tert-butyl 1-((isoquinolin-6-ylamino)methyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate
12046	tert-butyl 4-(((1,6-dimethyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-1-((isoquinolin-5-ylamino)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate
12047	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(3-(isoquinolin-5-yl)propanoyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one

Example No	Name
12048	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(3-(3-(difluoromethyl)phenyl)propanoyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one
12049	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(3-(3-chlorophenyl)propanoyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one
12050	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(3-(3-(trifluoromethyl)phenyl)propanoyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one
12051	3-(3-(1-(((1-aminoisoquinolin-5-yl)amino)methyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexan-2-yl)-3-oxopropyl)benzoic acid
12052	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(3-(quinolin-5-yl)propanoyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one
12053	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(3-(3-bromophenyl)propanoyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one
12054	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(3-(6-oxo-1,6-dihydropyridin-3-yl)propanoyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one
12055	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(3-(quinolin-7-yl)propanoyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one
12056	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(3-(3-(difluoromethoxy)phenyl)propanoyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one
12057	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(benzo[d]oxazol-2-yl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one
12058	1-(((1-aminoisoquinolin-5-yl)amino)methyl)-N-(2-fluorobenzyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxamide
12059	1-(((1-aminoisoquinolin-5-yl)amino)methyl)-N-(2-methoxyphenyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxamide
12060	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(5-phenylpyrimidin-2-yl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one

Example No	Name
12061	1-(((1-aminoisoquinolin-5-yl)amino)methyl)-N-(4-methoxyphenyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxamide
12062	1-(((1-aminoisoquinolin-5-yl)amino)methyl)-N-(4-methoxybenzyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxamide
12063	tert-butyl 1-((isoquinolin-7-ylamino)methyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate
12064	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(pyridin-3-yl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one
12065	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(pyridin-4-yl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one
12067	1-(((1-aminoisoquinolin-5-yl)amino)methyl)-N-(2-methoxybenzyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxamide
12068	1-(((1-aminoisoquinolin-5-yl)amino)methyl)-N-(2-fluorophenyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxamide
12069	1-(((1-aminoisoquinolin-5-yl)amino)methyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-N-(3-(trifluoromethyl)benzyl)-2-azabicyclo[2.1.1]hexane-2-carboxamide
12070	1-(((1-aminoisoquinolin-5-yl)amino)methyl)-N-(benzofuran-5-ylmethyl)-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxamide
12071	4-((1-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(4-methoxybenzoyl)-2-azabicyclo[2.1.1]hexan-4-yl)methoxy)-1-methylpyridin-2(1H)-one
12072	1-(((1-amino-6-fluoroisoquinolin-5-yl)amino)methyl)-N-benzyl-4-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxamide
13001	benzyl 4-(((1-aminoisoquinolin-5-yl)amino)methyl)-1-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate

Example No	Name
13002	benzyl 4-(((1-aminoisoquinolin-5-yl)amino)methyl)-1-(3-(trifluoromethyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine-7-carbonyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate
13003	4-((2-acetyl-4-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-azabicyclo[2.1.1]hexan-1-yl)methoxy)-1-methylpyridin-2(1H)-one
13004	2-chlorophenyl 4-(((1-aminoisoquinolin-5-yl)amino)methyl)-1-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate
13005	tert-butyl 4-(((1-aminoisoquinolin-5-yl)amino)methyl)-1-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate
13006	phenyl 4-(((1-aminoisoquinolin-5-yl)amino)methyl)-1-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate
13007	4-((4-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-azabicyclo[2.1.1]hexan-1-yl)methoxy)-1-methylpyridin-2(1H)-one
13008	4-((4-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(3-phenylpropanoyl)-2-azabicyclo[2.1.1]hexan-1-yl)methoxy)-1-methylpyridin-2(1H)-one
13009	pyridin-3-ylmethyl 4-(((1-aminoisoquinolin-5-yl)amino)methyl)-1-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate
13010	4-((4-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(3-(pyridin-3-yl)propanoyl)-2-azabicyclo[2.1.1]hexan-1-yl)methoxy)-1-methylpyridin-2(1H)-one
13011	4-(((1-aminoisoquinolin-5-yl)amino)methyl)-N-benzyl-N-methyl-1-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxamide
13012	4-(((1-aminoisoquinolin-5-yl)amino)methyl)-N-benzyl-1-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxamide
13013	pyridin-2-ylmethyl 4-(((1-aminoisoquinolin-5-yl)amino)methyl)-1-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate
13014	4-((4-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(phenethylsulfonyl)-2-azabicyclo[2.1.1]hexan-1-yl)methoxy)-1-methylpyridin-2(1H)-one
13015	4-((4-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(3-phenylpropyl)-2-azabicyclo[2.1.1]hexan-1-yl)methoxy)-1-methylpyridin-2(1H)-one
13016	4-((4-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(3-(pyridin-2-yl)propanoyl)-2-azabicyclo[2.1.1]hexan-1-yl)methoxy)-1-methylpyridin-2(1H)-one

Example No	Name
13017	4-((4-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(3-(2-chlorophenyl)propanoyl)-2-azabicyclo[2.1.1]hexan-1-yl)methoxy)-1-methylpyridin-2(1H)-one
13018	4-[[4-[[(1-aminoisoquinolin-5-yl)amino]methyl]-2-(1,3-benzoxazol-2-yl)-2-azabicyclo[2.1.1]hexan-1-yl]methoxy]-1-methylpyridin-2-one
13019	4-(((1-aminoisoquinolin-5-yl)amino)methyl)-1-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-N-phenyl-2-azabicyclo[2.1.1]hexane-2-carboxamide
13020	2-chlorobenzyl 4-(((1-aminoisoquinolin-5-yl)amino)methyl)-1-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate
13021	4-((4-(((1-aminoisoquinolin-5-yl)amino)methyl)-2-(2-phenylacetyl)-2-azabicyclo[2.1.1]hexan-1-yl)methoxy)-1-methylpyridin-2(1H)-one
13022	(1-methyl-1H-pyrazol-4-yl)methyl 4-(((1-aminoisoquinolin-5-yl)amino)methyl)-1-(((1-methyl-2-oxo-1,2-dihydropyridin-4-yl)oxy)methyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate

Table 15: ^{1}H NMR data of examples (solvent d6 DMSO unless otherwise indicated)

Example No	NMR write-up
1001	1.75 (6H, s), 4.04 (2H, s), 5.87 (1H, t, J = 5.9 Hz), 6.47 (2H, s), 6.56 (1H, dd, J = 7.4, 2.5 Hz), 6.65 (1H, d, J = 7.7 Hz), 6.87 (1H, d, J = 2.5 Hz), 7.11 - 7.16 (1H, m), 7.19 (1H, t, J = 8.0 Hz), 7.31 (1H, d, J = 8.3 Hz), 7.36 (1H, d, J = 1.3 Hz), 7.63 - 7.75 (2H, m), 8.35 (1H, dd, J = 7.4, 0.6 Hz)
1002	($CDCl_3$) 1.74 (6H, s), 2.04 - 2.17 (2H, m), 2.96 (1H, dd, J = 16.8, 5.8 Hz), 3.08 (1H, dd, J = 16.7, 4.7 Hz), 3.32 (2H, d, J = 3.6 Hz), 3.47 - 3.59 (2H, m), 3.84 - 3.96 (2H, m), 4.05 - 4.14 (1H, m), 4.22 (1H, s), 5.18 (2H, s), 6.71 (1H, dd, J = 7.7, 0.8 Hz), 6.79 (1H, d, J = 1.3 Hz), 6.93 (1H, dd, J = 6.2, 1.0 Hz), 6.99 (1H, d, J = 1.3 Hz), 7.11 (1H, dt, J = 8.5, 1.0 Hz), 7.34 (1H, t, J = 8.0 Hz), 7.91 (1H, d, J = 6.2 Hz)
1002.1	1.61 (6H, s), 1.96 - 2.07 (2H, m), 2.69 (1H, dd, J = 16.6, 5.5 Hz), 2.94 (1H, dd, J = 16.6, 4.6 Hz), 3.28 (2H, d, J = 5.8 Hz), 3.45 (2H, d, J = 2.8 Hz), 3.82 - 3.96 (3H, m), 5.81 (1H, t, J = 5.9 Hz), 6.46 (2H, s), 6.63 (1H, d, J = 7.5 Hz), 6.78 (1H, d, J = 1.3 Hz), 6.96 (1H, d, J = 1.3 Hz), 7.09 - 7.15 (1H, m), 7.19 (1H, t, J = 8.0 Hz), 7.30 (1H, d, J = 8.3 Hz), 7.70 (1H, d, J = 6.1 Hz)

Example No	NMR write-up
1002.2	1.61 (6H, s), 1.96 - 2.05 (2H, m), 2.69 (1H, dd, J = 16.5, 5.6 Hz), 2.94 (1H, dd, J = 16.6, 4.6 Hz), 3.28 (2H, d, J = 5.8 Hz), 3.45 (2H, d, J = 2.8 Hz), 3.82 - 3.96 (3H, m), 5.81 (1H, t, J = 5.7 Hz), 6.46 (2H, s), 6.62 (1H, d, J = 7.6 Hz), 6.78 (1H, d, J = 1.3 Hz), 6.96 (1H, d, J = 1.3 Hz), 7.12 (1H, d, J = 5.9 Hz), 7.19 (1H, t, J = 8.0 Hz), 7.30 (1H, d, J = 8.3 Hz), 7.70 (1H, d, J = 6.1 Hz)
1004	1.69 (6H, s), 2.56 (2H, s), 2.80 (2H, dd, J = 6.3, 4.7 Hz), 3.28 (2H, d, J = 5.6 Hz), 3.56 (2H, s), 3.91 (2H, t, J = 5.5 Hz), 5.81 (1H, t, J = 5.9 Hz), 6.47 (2H, s), 6.63 (1H, d, J = 7.6 Hz), 6.80 (1H, d, J = 1.2 Hz), 7.00 (1H, d, J = 1.2 Hz), 7.13 (1H, d, J = 6.1 Hz), 7.19 (1H, t, J = 8.0 Hz), 7.30 (1H, d, J = 8.3 Hz), 7.70 (1H, d, J = 6.1 Hz)
1005.1	0.89 (3H, d, J = 6.1 Hz), 0.94 (3H, d, J = 6.0 Hz), 1.45 (1H, d, J = 9.0 Hz), 1.51 (1H, d, J = 9.0 Hz), 1.58 (6H, s), 2.36 - 2.40 (1H, m), 2.41 (1H, d, J = 7.9 Hz), 2.46 - 2.49 (1H, m), 2.51 - 2.53 (2H, m), 2.55 (2H, d, J = 9.9 Hz), 2.68 (1H, dd, J = 9.3, 2.6 Hz), 3.13 (1H, s), 3.27 (2H, d, J = 5.7 Hz), 5.80 (1H, t, J = 5.8 Hz), 6.48 (2H, s), 6.61 (1H, d, J = 7.7 Hz), 7.09 - 7.15 (1H, m), 7.18 (1H, t, J = 8.0 Hz), 7.30 (1H, d, J = 8.3 Hz), 7.70 (1H, d, J = 6.0 Hz)
1006	(CD_3CN) 1.83 (6H, s), 2.31 (3H, d, J = 0.9 Hz), 3.40 (2H, d, J = 4.1 Hz), 4.06 (2H, s), 4.86 (1H, s), 5.57 (2H, s), 6.46 (1H, dd, J = 7.4, 2.5 Hz), 6.72 (1H, d, J = 2.5 Hz), 6.77 - 6.81 (1H, m), 7.05 (1H, dd, J = 6.1, 1.0 Hz), 7.20 (1H, dt, J = 8.3, 1.0 Hz), 7.30 (1H, s), 7.34 (1H, t, J = 8.0 Hz), 7.83 (1H, d, J = 6.2 Hz), 8.03 (1H, dd, J = 7.4, 0.7 Hz)
1009	1.73 (6H, s), 3.35 (2H, d, J = 5.9 Hz), 4.04 (2H, s), 6.12 (1H, d, J = 5.5 Hz), 6.47 (1H, t, J = 6.2 Hz), 6.53 - 6.60 (2H, m), 6.86 (1H, d, J = 2.5 Hz), 7.03 (1H, d, J = 3.4 Hz), 7.36 (1H, s), 7.71 (1H, s), 7.77 (1H, d, J = 5.5 Hz), 8.35 (1H, d, J = 7.4 Hz), 11.07 (1H, s)
1010	1.72 (6H, s), 4.04 (2H, s), 6.16 (1H, d, J = 5.8 Hz), 6.54 - 6.59 (3H, m), 6.86 (1H, d, J = 2.5 Hz), 7.36 (1H, d, J = 1.3 Hz), 7.71 (1H, s), 7.74 (1H, d, J = 5.7 Hz), 8.35 (1H, dd, J = 7.4, 0.7 Hz), 11.93 (1H, s)
1011	1.78 (6H, s), 3.27 (2H, d, J = 5.1 Hz), 4.07 (2H, s), 6.47 (1H, t, J = 5.5 Hz), 6.58 (1H, dd, J = 7.4, 2.5 Hz), 6.65 (1H, s), 6.89 (1H, d, J = 2.5 Hz), 7.14 (1H, dd, J = 8.9, 2.2 Hz), 7.37 (1H, s), 7.39 (1H, d, J = 5.9 Hz), 7.68 - 7.76 (2H, m), 8.16 (1H, d, J = 5.8 Hz), 8.36 (1H, d, J = 7.4 Hz), 8.84 (1H, s)
1012	1.72 (6H, s), 2.29 (3H, s), 3.32 (2H, s, obscured by H2O), 4.03 (2H, s), 6.08 (1H, d, J = 5.5 Hz), 6.16 - 6.26 (2H, m), 6.56 (1H, dd, J = 7.4, 2.5 Hz), 6.86 (1H, d, J = 2.5 Hz), 7.36 (1H, s), 7.67 (1H, d, J = 5.5 Hz), 7.71 (1H, s), 8.35 (1H, d, J = 7.4 Hz), 10.89 (1H, s)

Example No	NMR write-up
1013	1.88 (6H, s), 4.12 (2H, s), 4.16 (2H, s), 6.63 (1H, dd, J = 7.4, 2.4 Hz), 6.76 (2H, s), 6.92 (1H, d, J = 2.3 Hz), 7.07 (1H, d, J = 7.7 Hz), 7.13 (1H, d, J = 5.8 Hz), 7.35 (1H, t, J = 8.1 Hz), 7.38 (1H, d, J = 0.6 Hz), 7.70 - 7.74 (2H, m), 7.80 (1H, d, J = 5.9 Hz), 8.38 (1H, d, J = 7.4 Hz)
1014	($CDCl_3$) 1.78 (6H, s), 1.86 - 1.97 (2H, m), 2.90 - 2.99 (2H, m), 4.02 (2H, s), 5.28 (2H, d, J = 18.4 Hz), 6.53 (1H, dd, J = 7.4, 2.4 Hz), 6.84 (1H, d, J = 2.5 Hz), 7.15 (1H, dd, J = 6.2, 1.0 Hz), 7.36 - 7.45 (2H, m), 7.48 (2H, dd, J = 7.2, 1.3 Hz), 7.68 (1H, dt, J = 8.3, 1.3 Hz), 7.93 (1H, dd, J = 7.4, 0.7 Hz), 7.96 (1H, d, J = 6.2 Hz)
1015	2.20 (6H, d, J = 8.0 Hz), 3.83 - 4.01 (2H, m), 4.05 (2H, s), 4.16 (2H, s), 4.62 and 4.85 (total 2H, each s), 6.81 (2H, d, J = 6.6 Hz), 6.90 (1H, d, J = 12.7 Hz), 7.09 (1H, d, J = 7.8 Hz), 7.13 (1H, s), 7.18 (1H, d, J = 5.9 Hz), 7.36 (1H, t, J = 8.1 Hz), 7.73 (1H, d, J = 8.4 Hz), 7.80 (1H, d, J = 5.9 Hz)
1016	2.08 (6H, s), 2.95 - 3.20 (1H, m), 3.81 - 4.05 (5H, m), 4.58 - 4.79 (2H, m), 5.86 - 5.93 (1H, m), 6.52 (2H, s), 6.65 (1H, d, J = 7.7 Hz), 6.87 (1H, d, J = 9.3 Hz), 7.09 - 7.23 (3H, m), 7.33 (1H, d, J = 8.3 Hz), 7.72 (1H, d, J = 6.2 Hz)
1017	1.76 (6H, s), 3.96 (2H, s), 5.88 (1H, t, J = 5.7 Hz), 6.48 (2H, s), 6.66 (1H, d, J = 7.7 Hz), 7.00 (1H, dd, J = 9.7, 2.3 Hz), 7.14 (1H, d, J = 6.1 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.31 (1H, d, J = 8.3 Hz), 7.44 (1H, d, J = 9.9 Hz), 7.48 (1H, s), 7.72 (1H, d, J = 6.1 Hz), 7.80 (1H, s), 8.23 (1H, d, J = 2.3 Hz). 2H masked by water peak.
1018	1.76 (6H, s), 4.17 (2H, s), 5.86 (1H, t, J = 5.9 Hz), 6.46 (2H, s), 6.58 (1H, d, J = 7.5 Hz), 6.65 (1H, d, J = 7.7 Hz), 6.72 (1H, t, J = 7.1 Hz), 7.14 (1H, d, J = 6.1 Hz), 7.19 (1H, t, J = 8.0 Hz), 7.30 (1H, d, J = 8.3 Hz), 7.44 (1H, s), 7.71 (1H, d, J = 6.0 Hz), 7.89 (1H, s), 8.11 (1H, d, J = 6.7 Hz). 2H hidden by water peak (confirmed by COSY).
1019	1.71 (6H, s), 3.31 (3H,s), 3.95 (2H, s), 5.74 (1H, d, J = 2.7 Hz), 5.86 - 5.90 (2H, m), 6.48 (2H, s), 6.64 (1H, d, J = 7.7 Hz), 7.14 (1H, d, J = 6.2 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.31 (1H, d, J = 8.3 Hz), 7.53 (1H, d, J = 7.7 Hz), 7.71 (1H, d, J = 6.1 Hz). 2H masked by water peak.
1101	1.74 (6H, s), 4.05 (2H, s), 5.87 (1H, t, J = 5.8 Hz), 6.44 (1H, t, J = 2.2 Hz), 6.47 (2H, s), 6.65 (1H, d, J = 7.7 Hz), 7.14 (1H, d, J = 6.1 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.27 (1H, d, J = 2.3 Hz), 7.31 (1H, d, J = 8.3 Hz), 7.43 (1H, t, J = 2.9 Hz), 7.71 (1H, d, J = 6.1 Hz), 8.05 (1H, d, J = 2.5 Hz), 11.04 (1H, s). 2H masked by water peak
1105	1.73 (6H, s), 3.32 (2H, s), 3.98 (2H, s), 5.89 (1H, t, J = 5.8 Hz), 6.51 (2H, s), 6.63 - 6.67 (1H, m), 6.78 (1H, s), 6.97 (1H, s), 7.14 (1H, dd, J = 6.4, 0.9 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.31 (1H, d, J = 8.3 Hz), 7.46 (1H, s), 7.71 (1H, d, J = 6.1 Hz), 8.06 (1H, s), 12.21 (1H, s)

Example No	NMR write-up
1109	1.72 (6H, s), 3.32 (2H, d, J = 5.6 Hz), 4.05 (2H, s), 4.27 (2H, s), 5.88 (1H, t, J = 6.0 Hz), 6.49 (2H, s), 6.64 (1H, d, J = 7.7 Hz), 7.10 - 7.15 (3H, m), 7.19 (1H, t, J = 8.0 Hz), 7.31 (1H, d, J = 8.3 Hz), 7.40 - 7.47 (1H, m), 7.71 (1H, d, J = 6.0 Hz), 8.53 (1H, s)
1110	1.76 (6H, s), 3.32 (2H, s), 4.13 (2H, s), 5.73 (1H, t, J = 5.8 Hz), 6.53 (2H, s), 6.65 (1H, d, J = 7.7 Hz), 6.81 (1H, dd, J = 7.5, 2.6 Hz), 7.14-7.27 (3H, m), 7.31 (1H, d, J = 8.2 Hz), 7.70 (1H, d, J = 6.1 Hz), 8.30 (1H, s), 8.74 (1H, d, J = 7.5 Hz)
1113	1.64 (6H, s), 3.28 (2H, s), 3.86 (2H, s), 5.79 (1H, t, J = 5.7 Hz), 6.27 (1H, d, J = 2.2 Hz), 6.36 - 6.39 (3H, m), 6.57 (1H, d, J = 7.7 Hz), 6.97 (1H, d, J = 8.2 Hz), 7.06 (1H, d, J = 6.1 Hz), 7.12 (1H, t, J = 8.0 Hz), 7.23 (1H, d, J = 8.2 Hz), 7.64 (1H, d, J = 6.1 Hz), 10.21 (1H, s). 2H masked by water peak
1118	1.63 (6H, s), 2.63 (1H, dd, J = 16.5, 2.7 Hz), 3.01 (1H, dd, J = 16.5, 6.6 Hz), 3.28 (2H, d, J = 5.5 Hz), 3.40 - 3.48 (2H, m), 3.82 (1H, dd, J = 11.7, 2.6 Hz), 4.14 (1H, dd, J = 11.7, 5.9 Hz), 4.64 (1H, tt, J = 5.8, 2.6 Hz), 5.83 (1H, t, J = 5.9 Hz), 6.48 (2H, s), 6.62 (1H, d, J = 7.7 Hz), 6.85 (1H, d, J = 1.4 Hz), 7.03 (1H, d, J = 1.2 Hz), 7.10 - 7.14 (1H, m), 7.18 (1H, t, J = 8.0 Hz), 7.30 (1H, d, J = 8.3 Hz), 7.70 (1H, d, J = 6.1 Hz)
1125	1.74 (6H, s), 3.28 (2H, s), 4.02 (2H, s), 5.87 (1H, s), 6.49 (2H, s), 6.61 - 6.76 (2H, m), 6.87 (1H, s), 7.14 (1H, d, J = 6.2 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.31 (1H, d, J = 8.3 Hz), 7.57 (1H, d, J = 8.8 Hz), 7.71 (1H, d, J = 6.1 Hz), 7.90 (1H, s), 12.75 (1H, s)
1126	1.52 (6H, s), 3.26 (2H, d, J = 5.8 Hz), 4.11 (2H, s), 5.27 (1H, dd, J = 10.1, 2.2 Hz), 5.39 (1H, dd, J = 17.3, 2.2 Hz), 5.84 (1H, t, J = 5.8 Hz), 6.21 - 6.22 (2H, m), 6.45 (2H, s), 6.59 (1H, d, J = 7.7 Hz), 6.96 (1H, d, J = 0.7 Hz), 7.07 (1H, d, J = 0.8 Hz), 7.10 (1H, d, J = 6.2 Hz), 7.16 (1H, t, J = 8.0 Hz), 7.29 (1H, d, J = 8.2 Hz), 7.69 (1H, d, J = 6.1 Hz), 7.90 - 7.98 (1H, m)
1127	1.59 (6H, s), 3.27 (2H, d, J = 5.8 Hz), 3.94 (2H, s), 5.80 (1H, d, J = 2.1 Hz), 5.86 (1H, t, J = 5.7 Hz), 6.12 (1H, dd, J = 7.5, 2.1 Hz), 6.46 (2H, s), 6.59 (1H, d, J = 7.7 Hz), 7.10 (1H, d, J = 5.7 Hz), 7.17 (1H, t, J = 8.0 Hz), 7.23 (1H, d, J = 2.4 Hz), 7.29 (1H, d, J = 8.3 Hz), 7.39 (1H, d, J = 2.1 Hz), 7.69 (1H, d, J = 6.1 Hz), 7.88 (1H, d, J = 7.7 Hz)
1129	1.76 (6H, s), 3.17 (2H, d, J = 5.2 Hz), 4.06 (2H, s), 5.41 (1H, t, J = 5.7 Hz), 6.58 (1H, dd, J = 7.4, 2.5 Hz), 6.88 (1H, d, J = 2.5 Hz), 6.91 (1H, d, J = 2.6 Hz), 7.37 (1H, s), 7.41 (1H, d, J = 2.8 Hz), 7.72 (1H, s), 7.89 (1H, d, J = 2.6 Hz), 8.36 (1H, d, J = 7.4 Hz), 11.42 (1H, s)

Example No	NMR write-up
1130	1.59 (6H, s), 1.95 - 2.05 (2H, m), 2.68 (1H, dd, J = 16.6, 5.6 Hz), 2.94 (1H, dd, J = 16.5, 4.6 Hz), 3.30 (2H, d, J = 6.0 Hz), 3.41 - 3.48 (2H, m), 3.90 (3H, td, J = 6.2, 2.5 Hz), 6.14 (1H, d, J = 5.8 Hz), 6.53 (1H, s), 6.57 (1H, s), 6.78 (1H, d, J = 1.2 Hz), 6.96 (1H, d, J = 1.2 Hz), 7.73 (1H, d, J = 5.6 Hz), 11.93 (1H, s)
1131	($CDCl_3$)2.27 (6H, s), 4.11 (2H, s), 4.84 (1H, s), 5.21 (2H, s), 6.90 (1H, dd, J = 6.2, 0.9 Hz), 7.00 (1H, td, J = 10.1, 2.3 Hz), 7.09 (1H, dd, J = 7.8, 0.9 Hz), 7.19 (1H, d, J = 8.3 Hz), 7.38 (1H, t, J = 8.0 Hz), 7.47 - 7.61 (3H, m), 7.68 (1H, dd, J = 5.6, 2.3 Hz), 7.90 (1H, d, J = 6.2 Hz)
1132	2.07 (6H, s), 3.44 (2H, d, J = 5.7 Hz), 5.91 (1H, t, J = 5.8 Hz), 6.49 (2H, s), 6.67 (1H, d, J = 7.7 Hz), 7.16 (1H, d, J = 6.2 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.2 Hz), 7.72 (1H, d, J = 6.0 Hz), 7.78 (1H, t, J = 51.7 Hz), 7.90 (1H, dd, J = 9.6, 1.4 Hz), 7.99 (1H, dd, J = 9.6, 0.6 Hz), 9.03 (1H, s), 9.34 (1H, s)
1133	1.68 (s, 6H), 3.25 – 3.32 (m, 3H), 4.01 (s, 2H), 4.23 (s, 2H), 5.83 (t, J = 5.8 Hz, 1H), 6.47 (s, 2H), 6.60 (dd, J = 7.7, 0.9 Hz, 1H), 6.93 (dd, J = 8.4, 2.3 Hz, 1H), 7.00 – 7.05 (m, 1H), 7.09 (dd, J = 6.3, 0.9 Hz, 1H), 7.15 (t, J = 8.0 Hz, 1H), 7.23 – 7.30 (m, 1H), 7.47 (d, J = 8.4 Hz, 1H), 7.66 (d, J = 6.1 Hz, 1H), 8.22 (s, 1H)
1134	($CDCl_3$) 1.70 (6H, s), 2.26 (3H, s), 3.31 (5H, d, J = 4.8 Hz), 3.92 (2H, s), 5.64 (1H, d, J = 2.8 Hz), 5.79 - 5.91 (2H, m), 6.46 (2H, s), 6.64 (1H, d, J = 7.7 Hz), 7.13 (1H, d, J = 6.1 Hz), 7.19 (1H, t, J = 8.0 Hz), 7.30 (1H, d, J = 8.3 Hz), 7.71 (1H, d, J = 6.0 Hz)
1135	1.72 - 1.78 (6H, m), 3.33 - 3.37 (2H, m), 4.09 (2H, s), 5.83 - 5.90 (1H, m), 6.46 (2H, s), 6.65 (2H, d, J = 7.5 Hz), 7.01 (1H, s), 7.14 (1H, d, J = 4.7 Hz), 7.19 (1H, t, J = 7.0 Hz), 7.31 (1H, d, J = 7.7 Hz), 7.71 (1H, dd, J = 6.0, 2.0 Hz), 8.35 - 8.43 (1H, m), 9.01 (1H, d, J = 1.4 Hz)
2020	1.61 (2H, dd, J = 4.4, 1.7 Hz), 1.85 (2H, dd, J = 4.4, 1.7 Hz), 3.58 (2H, d, J = 5.9 Hz), 3.71 (2H, s), 4.25 (2H, s), 5.99 (1H, t, J = 5.9 Hz), 6.48 (2H, s), 6.59 (1H, dd, J = 7.4, 2.5 Hz), 6.68 (1H, d, J = 7.7 Hz), 6.93 (1H, d, J = 2.5 Hz), 7.17 (1H, d, J = 6.1 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.32 (1H, d, J = 8.3 Hz), 7.37 (1H, d, J = 1.3 Hz), 7.68 - 7.76 (2H, m), 8.36 (1H, d, J = 7.4 Hz)
2022	1.62 (2H, dd, J = 4.5, 1.7 Hz), 1.85 (2H, dd, J = 4.4, 1.7 Hz), 3.59 (2H, d, J = 5.9 Hz), 3.71 (2H, s), 4.17 (2H, s), 6.00 (1H, t, J = 6.0 Hz), 6.48 (2H, s), 6.69 (1H, d, J = 7.7 Hz), 7.02 (1H, dd, J = 9.7, 2.4 Hz), 7.13 - 7.27 (2H, m), 7.33 (1H, d, J = 8.3 Hz), 7.42 - 7.51 (2H, m), 7.72 (1H, d, J = 6.1 Hz), 7.81 (1H, t, J = 0.9 Hz), 8.24 - 8.30 (1H, m)
2204	1.63 (2H, dd, J = 4.5, 1.7 Hz), 1.87 (2H, dd, J = 4.6, 1.6 Hz), 3.59 (2H, d, J = 5.8 Hz), 3.71 (2H, s), 4.56 (2H, s), 6.06 (1H, t, J = 6.0 Hz), 6.69 - 6.81 (3H, m), 7.17 - 7.27 (3H, m), 7.36 (1H, d, J = 8.3 Hz), 7.46 - 7.74 (2H, m), 8.38 (1H, d, J = 9.9 Hz)

Example No	NMR write-up
2205	1.57 (2H, dd, J = 4.5, 1.7 Hz), 1.80 (2H, dd, J = 4.5, 1.7 Hz), 3.31 (3H, s), 3.56 (2H, d, J = 5.8 Hz), 3.68 (2H, s), 4.14 (2H, s), 5.79 (1H, d, J = 2.8 Hz), 5.90 (1H, dd, J = 7.5, 2.7 Hz), 5.98 (1H, t, J = 6.0 Hz), 6.48 (2H, s), 6.67 (1H, d, J = 7.7 Hz), 7.11 - 7.17 (1H, m), 7.20 (1H, t, J = 8.0 Hz), 7.32 (1H, d, J = 8.3 Hz), 7.53 (1H, d, J = 7.6 Hz), 7.72 (1H, d, J = 6.0 Hz)
2206	1.63 (2H, dd, J = 4.5, 1.7 Hz), 1.83 - 1.93 (2H, m), 3.59 (2H, d, J = 5.8 Hz), 3.72 (2H, s), 4.40 (2H, s), 6.02 (1H, t, J = 6.0 Hz), 6.54 (2H, s), 6.69 (1H, d, J = 7.7 Hz), 6.95 (1H, dd, J = 7.6, 2.4 Hz), 7.15 - 7.19 (1H, m), 7.22 (1H, t, J = 8.0 Hz), 7.34 (1H, d, J = 8.3 Hz), 7.39 (1H, dd, J = 2.4, 0.7 Hz), 7.72 (1H, d, J = 6.1 Hz), 8.45 (1H, d, J = 7.5 Hz)
2207	1.62 (2H, dd, J = 4.4, 1.7 Hz), 1.86 (2H, dd, J = 4.5, 1.7 Hz), 3.58 (2H, d, J = 5.9 Hz), 3.71 (2H, s), 4.35 (2H, s), 6.00 (1H, t, J = 6.0 Hz), 6.49 (2H, s), 6.68 (1H, d, J = 7.7 Hz), 6.84 (1H, dd, J = 7.5, 2.6 Hz), 7.14 - 7.28 (3H, m), 7.33 (1H, d, J = 8.3 Hz), 7.72 (1H, d, J = 6.1 Hz), 8.31 (1H, s), 8.74 (1H, d, J = 7.5 Hz)
2208	1.58 (2H, dd, J = 4.4, 1.7 Hz), 1.77 - 1.88 (2H, m), 3.56 (2H, d, J = 5.8 Hz), 3.69 (2H, s), 4.62 (2H, s), 5.98 (1H, t, J = 6.0 Hz), 6.48 (2H, s), 6.67 (1H, d, J = 7.7 Hz), 7.16 (1H, d, J = 6.1 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.32 (1H, d, J = 8.3 Hz), 7.72 (1H, d, J = 6.1 Hz), 9.10 (2H, s)
2210	1.62 (2H, dd, J = 4.4, 1.7 Hz), 1.85 (2H, dd, J = 4.5, 1.7 Hz), 3.58 (2H, d, J = 5.9 Hz), 3.71 (2H, s), 4.29 (2H, s), 5.99 (1H, t, J = 6.0 Hz), 6.48 (2H, s), 6.68 (1H, d, J = 7.7 Hz), 7.14 - 7.25 (2H, m), 7.33 (1H, d, J = 8.3 Hz), 7.45 (1H, dd, J = 9.7, 2.4 Hz), 7.69 - 7.77 (2H, m), 8.38 (1H, s), 8.70 (1H, dd, J = 2.5, 0.8 Hz)
2211	1.59 (2H, dd, J = 4.5, 1.7 Hz), 1.82 (2H, dd, J = 4.6, 1.6 Hz), 3.05 (3H, s), 3.57 (2H, d, J = 5.9 Hz), 3.70 (2H, s), 4.25 (2H, s), 4.35 (2H, s), 5.97 (1H, t, J = 6.0 Hz), 6.47 (2H, s), 6.67 (1H, d, J = 7.7 Hz), 7.09 - 7.17 (3H, m), 7.20 (1H, t, J = 8.0 Hz), 7.32 (1H, d, J = 8.3 Hz), 7.44 (1H, d, J = 8.2, 0.8 Hz), 7.72 (1H, d, J = 6.1 Hz)
2212	1.63 (2H, dd, J = 4.2, 1.1 Hz), 1.85 (2H, d, J = 4.4 Hz), 2.41 (3H, s), 3.59 (2H, d, J = 5.7 Hz), 3.72 (2H, s), 4.25 (2H, s), 6.00 (1H, t, J = 6.0 Hz), 6.51 (2H, s), 6.69 (1H, d, J = 7.8 Hz), 6.99 (1H, dd, J = 9.8, 2.2 Hz), 7.15 - 7.23 (2H, m), 7.28 - 7.34 (2H, m), 7.42 (1H, d, J = 9.7 Hz), 7.72 (1H, d, J = 6.1 Hz), 7.84 (1H, d, J = 2.1 Hz)
4401	1.98 (4H, tdd, J = 11.6, 9.5, 6.2 Hz), 2.77 (2H, dt, J = 14.5, 7.2 Hz), 3.29 (2H, dd, J = 7.4, 5.4 Hz), 4.08 (2H, d, J = 7.0 Hz), 5.92 (1H, t, J = 5.4 Hz), 6.47 (2H, s), 6.57 - 6.64 (2H, m), 6.93 (1H, d, J = 2.5 Hz), 7.15 (1H, d, J = 6.1 Hz), 7.22 (1H, t, J = 8.0 Hz), 7.32 (1H, d, J = 8.3 Hz), 7.38 (1H, d, J = 1.3 Hz), 7.67 - 7.75 (2H, m), 8.38 (1H, d, J = 7.4 Hz)

Example No	NMR write-up
5003	1.66 (2H, dt, J = 11.8, 9.0 Hz), 2.18 - 2.29 (2H, m), 2.56 - 2.74 (2H, m, J = 8.1 Hz), 3.21 (2H, t, J = 6.1 Hz), 3.98 (2H, d, J = 6.3 Hz), 5.88 (1H, t, J = 5.4 Hz), 6.47 (2H, d, J = 4.4 Hz), 6.55 - 6.63 (2H, m), 6.89 (1H, d, J = 2.5 Hz), 7.14 (1H, dd, J = 6.3, 0.9 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.31 (1H, d, J = 8.3 Hz), 7.37 (1H, d, J = 1.3 Hz), 7.67 - 7.75 (2H, m), 8.36 (1H, dd, J = 7.4, 0.6 Hz)
6601	($CDCl_3$) 1.82 - 1.97 (4H, m), 3.63 (2H, d, J = 5.2 Hz), 3.91 (2H, s), 4.28 (2H, s), 4.66 (1H, s), 5.10 (2H, s), 6.52 (1H, dd, J = 7.4, 2.4 Hz), 6.75 (1H, d, J = 7.7 Hz), 6.86 (1H, d, J = 2.4 Hz), 7.00 (1H, d, J = 6.1 Hz), 7.15 (1H, d, J = 8.3 Hz), 7.36 (1H, t, J = 8.0 Hz), 7.42 (1H, s), 7.49 (1H, d, J = 1.4 Hz), 7.94 (2H, dd, J = 6.8, 5.5 Hz)
6602	1.60 (2H, dd, J = 4.6, 1.7 Hz), 1.86 (2H, dd, J = 4.4, 1.7 Hz), 3.55 (2H, d, J = 5.8 Hz), 3.74 (2H, s), 4.24 (2H, s), 5.94 (1H, t, J = 6.0 Hz), 6.52 (2H, s), 6.70 (1H, d, J = 7.6 Hz), 7.01 (1H, dd, J = 9.7, 2.4 Hz), 7.11 (1H, d, J = 6.1 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.34 (1H, d, J = 8.3 Hz), 7.45 (1H, dt, J = 9.7, 0.8 Hz), 7.49 (1H, d, J = 1.1 Hz), 7.72 (1H, d, J = 6.1 Hz), 7.77 - 7.85 (1H, m), 8.28 (1H, dd, J = 2.5, 0.8 Hz)
6605	1.56 (2H, dd, J = 4.3, 1.3 Hz), 1.83 (2H, d, J = 5.1 Hz), 2.30 (3H, s), 3.55 (2H, d, J = 5.8 Hz), 3.72 (2H, s), 4.31 (2H, s), 6.13 (1H, d, J = 5.6 Hz), 6.23 (1H, s), 6.33 (1H, t, J = 6.3 Hz), 6.58 (1H, dd, J = 7.4, 2.5 Hz), 6.92 (1H, d, J = 2.4 Hz), 7.37 (1H, d, J = 1.0 Hz), 7.69 (1H, d, J = 5.5 Hz), 7.72 (1H, s), 8.36 (1H, J = 7.4 Hz), 10.93 (1H, s)
6606	1.56 (2H, dd, J = 4.2, 1.2 Hz), 1.84 (2H, d, J = 4.8 Hz), 3.57 (2H, d, J = 6.2 Hz), 3.72 (2H, s), 4.32 (2H, s), 6.22 (1H, d, J = 5.8 Hz), 6.57 (1H, d, J = 2.9 Hz), 6.59 (1H, s), 6.67 (1H, s), 6.92 (1H, d, J = 2.4 Hz), 7.37 (1H, d, J = 1.2 Hz), 7.72 (1H, s), 7.76 (1H, J = 5.6 Hz), 8.36 (1H, d, J = 7.4 Hz), 11.92 (1H, s)
6608	1.61 (2H, dd, J = 4.6, 1.7 Hz), 1.88 (2H, dd, J = 4.5, 1.7 Hz), 3.54 (2H, d, J = 5.9 Hz), 3.74 (2H, s), 4.65 (2H, s), 5.93 (1H, t, J = 6.0 Hz), 6.51 (2H, s), 6.69 (1H, d, J = 7.7 Hz), 7.07 - 7.12 (1H, m), 7.18 - 7.24 (2H, m), 7.33 (1H, d, J = 8.3 Hz), 7.53 (1H, t, J = 51.4 Hz), 7.72 (1H, d, J = 5.9 Hz), 8.37 (1H, d, J = 9.9 Hz)
6609	1.55 (2H, dd, J = 4.5, 1.7 Hz), 1.80 (2H, dd, J = 4.5, 1.7 Hz), 3.31 (10H, s), 3.53 (2H, d, J = 5.9 Hz), 3.68 (2H, s), 4.22 (2H, s), 5.79 (1H, d, J = 2.8 Hz), 5.86 - 5.96 (2H, m), 6.50 (2H, s), 6.68 (1H, d, J = 7.7 Hz), 7.10 (1H, d, J = 6.1 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.53 (1H, d, J = 7.5 Hz), 7.72 (1H, d, J = 6.0 Hz)

Example No	NMR write-up
6610	1.43 - 1.49 (2H, m), 1.67 (2H, d, J = 4.9 Hz), 1.90 (1H, dddd, J = 13.5, 9.1, 6.6, 2.1 Hz), 1.98 - 2.10 (1H, m), 2.59 - 2.74 (2H, m), 3.49 (2H, d, J = 5.9 Hz), 3.57 (2H, s), 3.68 - 3.82 (2H, m), 3.87 - 3.96 (2H, m), 3.99 - 4.08 (1H, m), 5.86 (1H, t, J = 6.0 Hz), 6.50 (2H, s), 6.66 (1H, d, J = 7.7 Hz), 6.77 (1H, d, J = 1.3 Hz), 6.92 (1H, d, J = 1.3 Hz), 7.08 (1H, d, J = 6.1 Hz), 7.19 (1H, t, J = 8.0 Hz), 7.32 (1H, d, J = 8.3 Hz), 7.71 (1H, d, J = 6.1 Hz)
6611	1.57 (2H, dd, J = 4.3, 1.8 Hz), 1.84 (2H, d, J = 4.7 Hz), 3.57 (2H, d, J = 6.2 Hz), 3.72 (2H, s), 4.24 (2H, s), 6.22 (1H, d, J = 5.7 Hz), 6.59 (1H, s), 6.69 (1H, s), 7.02 (1H, dd, J = 9.7, 2.4 Hz), 7.45 (1H, d, J = 9.7 Hz), 7.49 (1H, d, J = 1.1 Hz), 7.76 (1H, d, J = 5.6 Hz), 7.81 (1H, s), 8.28 (1H, d, J = 2.4 Hz) azaindole NH not observed
6612	1.60 (dd, J = 4.5, 1.7 Hz, 2H), 1.86 (dd, J = 4.5, 1.7 Hz, 2H), 3.52 – 3.59 (m, 2H), 3.73 (s, 2H), 4.57 (s, 2H), 5.92 (t, J = 6.1 Hz, 1H), 6.50 (s, 2H), 6.69 (d, J = 7.7 Hz, 1H), 6.86 (d, J = 9.7 Hz, 1H), 7.10 (d, J = 6.1 Hz, 1H), 7.21 (dd, J = 9.4, 6.6 Hz, 1H), 7.33 (d, J = 8.3 Hz, 1H), 7.59 (d, J = 1.2 Hz, 1H), 7.72 (dd, J = 6.2, 2.3 Hz, 1H), 7.98 (d, J = 9.7 Hz, 1H), 8.02 (d, J = 1.1 Hz, 1H)
6613	1.60 (2H, dd, J = 4.4, 1.7 Hz), 1.86 (2H, dd, J = 4.4, 1.7 Hz), 3.55 (2H, d, J = 5.9 Hz), 3.74 (2H, s), 4.34 (2H, s), 5.95 (1H, t, J = 6.0 Hz), 6.58 (2H, s), 6.66 - 6.74 (2H, m), 6.89 - 7.19 (3H, m), 7.22 (1H, t, J = 8.0 Hz), 7.35 (1H, d, J = 8.3 Hz), 7.72 (1H, d, J = 6.1 Hz), 8.04 (1H, t, J = 2.1 Hz), 8.40 (1H, d, J = 7.5 Hz)
6614	1.59 (2H, dd, J = 4.4, 1.4 Hz), 1.85 (2H, d, J = 4.5, 1.0 Hz), 3.54 (2H, d, J = 5.7 Hz), 3.71 (2H, s), 4.63 (2H, s), 5.91 (1H, t, J = 5.9 Hz), 6.52 (2H, s), 6.58 (1H, d, J = 7.2 Hz), 6.68 (1H, d, J = 7.7 Hz), 7.10 (1H, d, J = 6.2 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.39 (1H, d, J = 1.4 Hz), 7.65 (1H, d, J = 1.5 Hz), 7.71 (1H, d, J = 6.1 Hz), 8.21 (1H, s), 8.73 (1H, d, J = 7.2 Hz) acid proton missing
6615	1.61 (2H, dd, J = 4.3, 1.2 Hz), 1.87 (2H, d, J = 4.4, 0.8 Hz), 3.55 (2H, d, J = 5.9 Hz), 3.74 (2H, s), 4.60 (2H, s), 5.92 (1H, t, J = 6.0 Hz), 6.49 (2H, s), 6.69 (1H, d, J = 7.7 Hz), 7.08 (1H, d, J = 4.7 Hz), 7.10 (1H, s), 7.21 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.72 (1H, d, J = 6.1 Hz), 8.11 (1H, d, J = 9.8 Hz), 8.70 (1H, s)
6616	1.57 (2H, dd, J = 4.5, 1.7 Hz), 1.83 (2H, dd, J = 4.5, 1.7 Hz), 3.53 (2H, d, J = 5.8 Hz), 3.72 (2H, s), 4.47 (2H, s), 5.90 (1H, t, J = 6.0 Hz), 6.49 (2H, s), 6.69 (1H, d, J = 7.7 Hz), 7.09 (1H, d, J = 6.1 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.71 (1H, d, J = 6.1 Hz), 7.78 (1H, d, J = 1.0 Hz), 8.02 (1H, d, J = 0.9 Hz), 8.24 (1H, d, J = 1.4 Hz), 8.81 (1H, d, J = 1.3 Hz)

Example No	NMR write-up
6617	1.59 (2H, dd, J = 4.4, 1.7 Hz), 1.85 (2H, dd, J = 4.7, 1.6 Hz), 2.42 (3H, d, J = 0.9 Hz), 3.55 (2H, d, J = 5.9 Hz), 3.73 (2H, s), 4.21 (2H, s), 5.94 (1H, t, J = 6.1 Hz), 6.50 (2H, s), 6.69 (1H, d, J = 7.7 Hz), 6.86 (1H, dd, J = 2.4, 1.2 Hz), 7.07 - 7.13 (1H, m), 7.21 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.44 (1H, d, J = 1.1 Hz), 7.72 (1H, d, J = 6.1 Hz), 7.78 (1H, d, J = 1.1 Hz), 8.10 - 8.14 (1H, m)
6618	1.58 (2H, dd, J = 4.5, 1.7 Hz), 1.84 (2H, dd, J = 4.6, 1.7 Hz), 3.54 (2H, d, J = 5.6 Hz), 3.72 (2H, s), 4.28 (2H, s), 4.33 (2H, s), 5.94 (1H, t, J = 6.0 Hz), 6.59 (2H, s), 6.70 (1H, d, J = 7.7 Hz), 7.01 (1H, dd, J = 8.4, 2.3 Hz), 7.08 - 7.16 (2H, m), 7.21 (1H, t, J = 8.0 Hz), 7.34 (1H, d, J = 8.3 Hz), 7.53 (1H, d, J = 8.4 Hz), 7.71 (1H, d, J = 6.1 Hz), 8.27 (1H, s), 8.31 (1H, s) formic acid OH was not observed
6619	1.79 (2H, dd, J = 4.2, 1.1 Hz), 2.05 (2H, d, J = 4.1 Hz), 3.42 (2H, s), 3.84 (2H, s), 4.43 (2H, s), 5.59 (1H, s), 6.82 (2H, s), 7.03 (1H, dd, J = 9.2, 2.1 Hz), 7.19 - 7.23 (2H, m), 7.41 - 7.46 (3H, m), 7.55 (1H, d, J = 1.7 Hz), 7.78 (1H, s), 7.81 (1H, d, J = 8.4 Hz), 7.88 (1H, d, J = 5.9 Hz), 8.39 (2H, s) two acid protons missing
6620	1.61 (2H, dd, J = 4.4, 1.7 Hz), 1.88 (2H, d, J = 4.5 Hz), 3.56 (2H, d, J = 5.8 Hz), 3.75 (2H, s), 4.35 (2H, s), 5.94 (1H, t, J = 6.1 Hz), 6.51 (2H, s), 6.70 (1H, d, J = 7.7 Hz), 7.10 (1H, d, J = 6.2 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.31 - 7.41 (2H, m), 7.56 - 7.84 (2H, m), 7.87 (1H, d, J = 9.9 Hz), 8.12 (1H, d, J = 2.2 Hz)
6621	1.58 (2H, dd, J = 4.4, 1.7 Hz), 1.84 (2H, dd, J = 4.4, 1.7 Hz), 3.02 (3H, s), 3.54 (2H, d, J = 5.9 Hz), 3.72 (2H, s), 4.35 (4H, d, J = 11.4 Hz), 5.92 (1H, t, J = 6.0 Hz), 6.50 (2H, s), 6.69 (1H, d, J = 7.7 Hz), 7.00 (1H, dd, J = 8.4, 2.3 Hz), 7.10 (1H, d, J = 6.1 Hz), 7.14 (1H, d, J = 2.2 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.52 (1H, d, J = 8.3 Hz), 7.72 (1H, d, J = 6.1 Hz)
6622	1.63 (2H, dd, J = 4.2, 1.3 Hz), 1.88 (2H, dd, J = 4.4, 0.9 Hz), 2.19 (3H, s), 3.56 (2H, d, J = 5.9 Hz), 3.76 (2H, s), 4.22 (2H, s), 5.90 (1H, t, J = 6.0 Hz), 6.51 (2H, s), 6.72 (1H, d, J = 7.7 Hz), 7.11 (1H, d, J = 6.2 Hz), 7.22 (1H, t, J = 8.0 Hz), 7.32 - 7.35 (2H, m), 7.39 (1H, d, J = 0.6 Hz), 7.71 - 7.73 (2H, m), 8.19 (1H, s)
6623	($CDCl_3$) 1.85 (2H, dd, J = 4.7, 1.5 Hz), 1.92 (3H, d, J = 4.8 Hz), 3.60 (2H, s), 3.90 (2H, s), 4.53 (2H, s), 6.77 - 6.84 (2H, m), 6.97 (1H, dd, J = 6.5, 0.9 Hz), 7.16 (1H, d, J = 8.3 Hz), 7.40 (1H, t, J = 8.0 Hz), 7.52 - 7.61 (2H, m), 7.74 (1H, d, J = 6.5 Hz), 8.80 (1H, d, J = 1.3 Hz) NH2 protons not observed

Example No	NMR write-up
6624	1.61 (2H, dd, J = 4.3, 1.3 Hz), 1.88 (2H, d, J = 5.3 Hz), 2.41 (3H, s), 3.56 (2H, d, J = 5.8 Hz), 3.75 (2H, s), 4.32 (2H, s), 5.93 (1H, t, J = 5.9 Hz), 6.54 (2H, s), 6.71 (1H, d, J = 7.7 Hz), 6.99 (1H, dd, J = 9.7, 2.3 Hz), 7.11 (1H, d, J = 6.2 Hz), 7.22 (1H, t, J = 8.0 Hz), 7.29 (1H, d, J = 0.7 Hz), 7.34 (1H, d, J = 7.7 Hz), 7.43 (1H, d, J = 9.9 Hz), 7.72 (1H, d, J = 6.1 Hz), 7.83 (1H, d, J = 2.1 Hz), 8.19 (2H, s) two acid protons missing
6625	1.60 (2H, dd, J = 4.3, 1.7 Hz), 1.86 (2H, dd, J = 4.3, 1.7 Hz), 3.55 (2H, d, J = 5.9 Hz), 3.74 (2H, s), 4.30 (2H, s), 5.93 (1H, t, J = 6.0 Hz), 6.51 (2H, s), 6.70 (1H, d, J = 7.7 Hz), 7.01 (1H, dd, J = 9.9, 2.4 Hz), 7.11 (1H, d, J = 6.2 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.28 (1H, d, J = 7.2 Hz), 7.34 (1H, d, J = 8.3 Hz), 7.42 (1H, dd, J = 9.8, 2.0 Hz), 7.72 (1H, d, J = 6.1 Hz), 7.91 (1H, d, J = 2.3 Hz)
6626	1.59 (2H, dd, J = 4.3, 1.4 Hz), 1.84 (2H, dd, J = 4.3, 1.0 Hz), 2.46 (3H, s), 3.55 (2H, d, J = 5.7 Hz), 3.74 (2H, s), 4.29 (2H, s), 5.93 (1H, t, J = 6.0 Hz), 6.53 (2H, s), 6.70 (1H, d, J = 7.7 Hz), 7.11 (1H, d, J = 6.2 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.29 - 7.34 (2H, m), 7.45 (1H, d, J = 9.6 Hz), 7.61 (1H, d, J = 0.9 Hz), 7.71 (1H, d, J = 6.3 Hz), 7.76 (1H, s), 8.19 (1H, s) one acid proton missing
6627	1.61 (2H, dd, J = 4.5, 1.7 Hz), 1.87 (2H, dd, J = 4.4, 1.7 Hz), 3.56 (2H, d, J = 5.9 Hz), 3.75 (2H, s), 4.27 (2H, s), 5.94 (1H, t, J = 6.1 Hz), 6.51 (2H, d, J = 3.2 Hz), 6.70 (1H, d, J = 7.8 Hz), 7.11 (1H, dd, J = 6.5, 2.0 Hz), 7.18 - 7.26 (2H, m), 7.34 (1H, d, J = 8.4 Hz), 7.58 (1H, d, J = 9.8 Hz), 7.73 (1H, d, J = 6.1 Hz), 8.31 (1H, dd, J = 2.4, 0.8 Hz), 8.36 (1H, t, J = 1.0 Hz)
6628	1.57 (2H, dd, J = 4.5, 1.7 Hz), 1.84 (2H, dd, J = 4.4, 1.7 Hz), 3.05 (3H, s), 3.54 (2H, d, J = 5.8 Hz), 3.72 (2H, s), 4.34 (4H, d, J = 12.0 Hz), 5.91 (1H, t, J = 6.1 Hz), 6.50 (2H, s), 6.69 (1H, d, J = 7.6 Hz), 7.08 - 7.18 (3H, m), 7.21 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.44 (1H, d, J = 8.2 Hz), 7.72 (1H, d, J = 6.0 Hz)
6629	δ 1.60 (2H, dd, J = 4.4, 1.3 Hz), 1.86 (2H, dd, J = 4.5, 0.8 Hz), 3.56 (2H, d, J = 7.2 Hz), 3.73 (2H, s), 4.38 (2H, s), 5.96 (1H, t, J = 5.7 Hz), 6.63 (2H, s), 6.66 - 6.72 (2H, m), 7.07 - 7.13 (2H, m), 7.19 - 7.24 (1H, m), 7.34 (1H, d, J = 8.2 Hz), 7.72 (1H, d, J = 6.1 Hz), 8.18 (1H, s), 8.39 (1H, d, J = 7.3 Hz), 9.02 (1H, s)
6630	1.55 - 1.65 (2H, m), 1.87 (2H, dd, J = 4.5, 1.7 Hz), 3.55 (2H, d, J = 5.9 Hz), 3.75 (2H, s), 4.31 (2H, s), 5.94 (1H, t, J = 6.0 Hz), 6.51 (2H, s), 6.69 (1H, d, J = 7.7 Hz), 7.10 (1H, d, J = 6.1 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.49 (1H, dd, J = 2.3, 1.0 Hz), 7.62 (1H, d, J = 1.1 Hz), 7.72 (1H, d, J = 6.0 Hz), 7.99 (1H, d, J = 1.2 Hz), 8.61 (1H, d, J = 2.3 Hz)

Example No	NMR write-up
6631	1.60 (2H, dd, J = 4.5, 1.7 Hz), 1.83 - 1.88 (2H, m), 3.56 (2H, d, J = 5.9 Hz), 3.74 (2H, s), 3.89 (3H, s), 4.21 (2H, s), 5.96 (1H, t, J = 6.1 Hz), 6.41 (1H, d, J = 2.0 Hz), 6.51 (2H, d, J = 5.1 Hz), 6.69 (1H, d, J = 7.7 Hz), 7.11 (1H, d, J = 6.3 Hz), 7.21 (1H, td, J = 7.8, 4.0 Hz), 7.34 (1H, d, J = 8.2 Hz), 7.39 (1H, d, J = 1.1 Hz), 7.69 - 7.75 (1H, m), 7.77 (1H, d, J = 1.1 Hz), 7.89 (1H, d, J = 2.0 Hz)
6633	1.59 (2H, dd, J = 4.5, 1.7 Hz), 1.84 (2H, dd, J = 4.6, 1.7 Hz), 2.29 (3H, d, J = 0.7 Hz), 3.58 (2H, d, J = 5.6 Hz), 3.73 (2H, s), 4.22 (2H, s), 6.28 (1H, t, J = 6.0 Hz), 6.90 (1H, d, J = 7.9 Hz), 6.98 (1H, dd, J = 9.7, 2.4 Hz), 7.28 - 7.40 (3H, m), 7.49 (1H, d, J = 8.3 Hz), 7.56 (1H, t, J = 0.8 Hz), 7.59 - 7.73 (3H, m), 8.14 (2H, s), 8.21 (1H, dd, J = 2.5, 0.8 Hz)
6634	1.61 (2H, dd, J = 4.5, 1.7 Hz), 1.86 (2H, dd, J = 4.4, 1.7 Hz), 3.56 (2H, d, J = 5.7 Hz), 3.74 (2H, s), 4.26 (2H, s), 5.99 (1H, t, J = 6.1 Hz), 6.69 (2H, s), 6.73 (1H, d, J = 7.8 Hz), 7.13 (1H, d, J = 6.2 Hz), 7.18 (1H, dd, J = 9.9, 2.2 Hz), 7.23 (1H, t, J = 8.0 Hz), 7.36 (1H, d, J = 8.3 Hz), 7.66 - 7.74 (2H, m), 8.16 (1H, s), 8.25 (1H, d, J = 2.2 Hz), 9.09 (1H, s)
6635	1.46 (2H, dd, J = 4.6, 1.7 Hz), 1.67 (2H, d, J = 5.0 Hz), 3.46 (2H, d, J = 5.8 Hz), 3.55 (2H, s), 3.83 (2H, s), 5.84 (1H, t, J = 6.0 Hz), 6.51 (2H, s), 6.63 (1H, d, J = 7.7 Hz), 7.04 - 7.14 (3H, m), 7.18 (1H, t, J = 8.0 Hz), 7.31 (1H, d, J = 8.3 Hz), 7.67 (2H, d, J = 8.2 Hz), 8.30 (1H, s)
6636	1.59 (2H, dd, J = 4.4, 1.7 Hz), 1.85 (2H, dd, J = 4.4, 1.7 Hz), 3.52 - 3.58 (2H, m), 3.73 (2H, s), 4.45 (2H, s), 5.93 (1H, t, J = 6.1 Hz), 6.53 (2H, d, J = 5.6 Hz), 6.70 (1H, d, J = 7.7 Hz), 7.07 - 7.14 (1H, m), 7.17 - 7.25 (1H, m), 7.29 - 7.36 (2H, m), 7.69 - 7.77 (2H, m), 8.30 (2H, s)
6637	1.57 (2H, dd, J = 4.4, 1.7 Hz), 1.83 (2H, dd, J = 4.5, 1.7 Hz), 2.83 (2H, t, J = 6.6 Hz), 3.29 - 3.32 (2H, m), 3.54 (2H, d, J = 5.9 Hz), 3.71 (2H, s), 4.30 (2H, s), 5.93 (1H, t, J = 6.0 Hz), 6.51 (2H, s), 6.69 (1H, d, J = 7.7 Hz), 6.82 - 6.91 (2H, m), 7.10 (1H, d, J = 6.1 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.69 - 7.77 (3H, m)
6638	1.61 (2H, dd, J = 4.5, 1.7 Hz), 1.87 (2H, dd, J = 4.5, 1.7 Hz), 3.55 (2H, d, J = 5.9 Hz), 3.73 (2H, s), 4.60 (2H, s), 5.94 (1H, t, J = 6.0 Hz), 6.51 (2H, s), 6.69 (1H, d, J = 7.7 Hz), 7.05 (1H, d, J = 9.8 Hz), 7.10 (1H, d, J = 6.2 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.72 (1H, d, J = 6.1 Hz), 8.24 (1H, dd, J = 9.8, 0.8 Hz), 9.39 (1H, d, J = 0.8 Hz)
6639	0.60 - 0.64 (2H, m), 0.96 - 1.00 (2H, m), 1.61 (2H, dd, J = 4.2, 1.3 Hz), 1.97 (2H, d, J = 5.1 Hz), 1.92 - 1.99 (1H, m), 3.56 (2H, d, J = 5.8 Hz), 3.75 (2H, s), 4.34 (2H, s), 5.95 (1H, t, J = 5.9 Hz), 6.55 (2H, s), 6.71 (1H, d, J = 7.8 Hz), 7.02 (1H, dd, J = 9.7, 2.3 Hz), 7.11 (1H, d, J = 6.2 Hz), 7.20 - 7.24 (2H, m), 7.34 (1H, d, J = 8.3 Hz), 7.42 (1H, d, J = 9.7 Hz), 7.72 (1H, d, J = 6.1 Hz), 7.99 (1H, d, J = 2.0 Hz), 8.25 (2H, s) two acid protons missing

Example No	NMR write-up
6640	1.57 (2H, d, J = 3.4 Hz), 1.83 (2H, d, J = 3.5 Hz), 2.90 (2H, t, J = 6.5 Hz), 2.97 (3H, s), 3.48 (2H, t, J = 6.6 Hz), 3.55 (2H, d, J = 4.7 Hz), 3.71 (2H, s), 4.30 (2H, s), 6.09 (1H,s), 6.77 (1H, d, J = 7.8 Hz), 6.83 - 6.88 (2H, m), 7.02 (2H, s), 7.19 (1H, d, J = 6.3 Hz), 7.27 (1H, t, J = 7.9 Hz), 7.40 (1H, d, J = 8.2 Hz), 7.69 (1H, d, J = 6.2 Hz), 7.75 (1H, d, J = 8.6 Hz)
6641	1.29 (6H, d, J = 6.9 Hz), 1.60 (2H, dd, J = 4.4, 1.7 Hz), 1.86 (2H, dd, J = 4.4, 1.7 Hz), 3.46 (1H, p, J = 6.9 Hz), 3.55 (2H, d, J = 6.0 Hz), 3.74 (2H, s), 4.21 (2H, s), 5.95 (1H, t, J = 6.0 Hz), 6.51 (2H, s), 6.69 (1H, d, J = 7.7 Hz), 6.79 (1H, d, J = 2.2 Hz), 7.11 (1H, d, J = 6.2 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.44 (1H, d, J = 1.1 Hz), 7.72 (1H, d, J = 6.1 Hz), 7.78 (1H, d, J = 1.1 Hz), 8.11 (1H, d, J = 2.3 Hz)
6642	1.57 (2H, dd, J = 4.5, 1.7 Hz), 1.84 (2H, dd, J = 4.5, 1.7 Hz), 3.54 (2H, d, J = 5.9 Hz), 3.72 (2H, s), 4.30 (4H, d, J = 20.6 Hz), 5.93 (1H, t, J = 6.0 Hz), 6.51 (2H, s), 6.69 (1H, d, J = 7.7 Hz), 7.10 (1H, d, J = 6.1 Hz), 7.12 - 7.17 (2H, m), 7.21 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.44 (1H, d), 7.71 (1H, d, J = 6.0 Hz), 8.54 (1H, s)
6643	1.59 (2H, dd, J = 4.3, 1.2 Hz), 1.85 (2H, d, J = 4.5 Hz), 3.45 (3H, s), 3.61 (2H, d, J = 5.9 Hz), 3.73 (2H, s), 4.37 (2H, s), 6.48 - 6.53 (2H, m), 7.02 - 7.06 (2H, m), 7.12 (1H, d, J = 2.4 Hz), 7.41 - 7.49 (3H, m), 7.58 - 7.62 (2H, m), 8.09 (1H, d, J = 8.9 Hz), 8.35 (2H, s), 12.90 (1H, s)
6644	1.61 (2H, dd, J = 4.5, 1.7 Hz), 1.87 (2H, dd, J = 4.5, 1.7 Hz), 3.56 (2H, d, J = 5.9 Hz), 3.75 (2H, s), 4.32 (2H, s), 5.93 (1H, t, J = 6.0 Hz), 6.50 (2H, s), 6.70 (1H, d, J = 7.7 Hz), 7.11 (1H, d, J = 6.1 Hz), 7.18 - 7.28 (2H, m), 7.34 (1H, d, J = 8.3 Hz), 7.44 (1H, t, J = 53.3 Hz), 7.61 - 7.64 (1H, m), 7.72 (1H, d, J = 6.1 Hz), 7.85 (1H, t, J = 2.0 Hz), 8.07 (1H, dd, J = 2.4, 0.8 Hz)
6645	1.44 (2H, dd, J = 4.5, 1.7 Hz), 1.62 (2H, dd, J = 4.5, 1.6 Hz), 3.47 (2H, d, J = 5.9 Hz), 3.50 (2H, s), 4.45 (2H, s), 5.84 - 5.91 (1H, m), 6.19 - 6.21 (1H, m), 6.48 (2H, s), 6.63 (1H, d, J = 7.4 Hz), 7.06 (1H, d, J = 5.9 Hz), 7.19 (1H, t, J = 8.0 Hz), 7.32 (1H, d, J = 8.4 Hz), 7.40 (1H, dd, J = 1.8, 0.7 Hz), 7.65 (1H, dd, J = 2.2, 0.7 Hz), 7.70 (1H, d, J = 6.1 Hz)
6646	1.45 (2H, dd, J = 4.5, 1.6 Hz), 1.62 (2H, dd, J = 4.5, 1.6 Hz), 3.46 - 3.51 (4H, m), 4.32 (2H, s), 5.90 (1H, t, J = 5.8 Hz), 6.52 (2H, s), 6.64 (1H, d, J = 7.5 Hz), 6.86 (1H, s), 7.07 (2H, d, J = 6.4 Hz), 7.19 (1H, t, J = 8.0 Hz), 7.32 (1H, d, J = 8.3 Hz), 7.55 (1H, s), 7.70 (1H, d, J = 6.1 Hz)
6647	1.48 (2H, dd, J = 4.6, 1.7 Hz), 1.64 - 1.70 (2H, m), 3.48 (2H, d, J = 6.0 Hz), 3.54 (2H, s), 4.78 (2H, s), 5.87 (1H, t, J = 5.9 Hz), 6.47 (2H, s), 6.63 (1H, d, J = 7.6 Hz), 7.06 (1H, d, J = 5.6 Hz), 7.19 (1H, t, J = 8.0 Hz), 7.32 (1H, d, J = 8.3 Hz), 7.70 (1H, d, J = 6.1 Hz), 7.76 (2H, s)

Example No	NMR write-up
6648	1.47 (2H, dd, J = 4.5, 1.6 Hz), 1.63 (2H, dd, J = 4.4, 1.5 Hz), 3.50 (2H, d, J = 6.0 Hz), 3.53 (2H, s), 4.75 (2H, s), 6.02 (1H, t, J = 5.8 Hz), 6.71 (1H, d, J = 7.7 Hz), 6.91 (2H, s), 7.14 (1H, d, J = 6.3 Hz), 7.25 (1H, t, J = 8.0 Hz), 7.38 (1H, d, J = 8.3 Hz), 7.68 (1H, d, J = 5.9 Hz), 7.70 (1H, d, J = 0.9 Hz), 8.07 (1H, d, J = 0.9 Hz)
6649	1.50 (2H, dd, J = 4.4, 1.6 Hz), 1.69 (2H, dd, J = 4.4, 1.5 Hz), 1.84 - 1.93 (2H, m), 2.18 (2H, t, J = 8.0 Hz), 3.33 (2H, s), 3.47 (2H, s), 3.50 (2H, d, J = 5.9 Hz), 3.52 (2H, s), 5.96 (1H, t, J = 5.9 Hz), 6.73 (1H, d, J = 7.7 Hz), 6.84 (2H, s), 7.15 (1H, d, J = 6.4 Hz), 7.25 (1H, t, J = 8.0 Hz), 7.38 (1H, d, J = 8.3 Hz), 7.69 (1H, d, J = 6.3 Hz)
6650	1.39 (6H, s), 1.58 (2H, d, J = 3.3 Hz), 1.85 (2H, d, J = 4.4 Hz), 3.55 (2H, d, J = 5.8 Hz), 3.73 (2H, s), 4.34 (2H, s), 5.94 (1H, t, J = 6.1 Hz), 6.50 (2H, s), 6.69 (1H, d, J = 7.7 Hz), 6.95 (1H, dd, J = 8.4, 2.1 Hz), 7.10 (1H, d, J = 6.1 Hz), 7.19 (1H, d, J = 2.2 Hz), 7.22 (1H, d, J = 7.9 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.46 (1H, d, J = 8.4 Hz), 7.72 (1H, d, J = 6.1 Hz), 8.39 (1H, s)
6651	1.46 - 1.56 (2H, m), 1.76 - 1.80 (2H, m), 2.80 (2H, s), 3.70 (2H, s), 4.42 (2H, s), 5.21 (2H, s), 6.75 (1H, s), 7.14 (1H, dd, J = 8.4, 2.3 Hz), 7.26 (1H, d, J = 2.2 Hz), 7.71 - 7.79 (2H, m), 8.19 (1H, d, J = 5.4 Hz)
6653	1.58 (2H, dd, J = 4.5, 1.7 Hz), 1.81 - 1.87 (2H, m), 1.97 - 2.09 (2H, m), 2.45 - 2.49 (2H, m), 3.54 (2H, d, J = 5.9 Hz), 3.71 (2H, s), 3.79 (2H, t, J = 7.0 Hz), 4.24 (2H, s), 5.89 (1H, t, J = 6.0 Hz), 6.48 (2H, s), 6.66 - 6.74 (2H, m), 7.10 (1H, d, J = 5.9 Hz), 7.16 (1H, ddd, J = 8.2, 2.0, 1.0 Hz), 7.18 - 7.26 (2H, m), 7.30 - 7.35 (2H, m), 7.72 (1H, d, J = 6.1 Hz)
6654	1.54 (2H, dd, J = 4.5, 1.7 Hz), 1.75 - 1.87 (4H, m), 2.12 (2H, t, J = 8.0 Hz), 3.51 (2H, t, J = 6.9 Hz), 3.55 (2H, d, J = 6.2 Hz), 3.70 (2H, s), 4.21 (2H, s), 5.97 - 6.05 (1H, m), 6.48 (2H, s), 6.67 (1H, d, J = 7.7 Hz), 6.93 (1H, td, J = 7.6, 1.3 Hz), 7.05 (1H, dd, J = 8.4, 1.2 Hz), 7.12 (1H, d, J = 5.8 Hz), 7.15 (1H, dd, J = 7.7, 1.7 Hz), 7.18 - 7.28 (2H, m), 7.33 (1H, d, J = 8.4 Hz), 7.72 (1H, d, J = 6.1 Hz)
6656	1.61 (2H, d, J = 4.4 Hz), 1.89 (2H, d, J = 4.5 Hz), 2.14 (3H, d, J = 1.1 Hz), 2.42 (3H, s), 3.41 (2H, d, J = 6.0 Hz), 3.56 (3H, s), 3.75 (2H, s), 4.33 (2H, s), 5.21 (1H, t, J = 6.0 Hz), 6.45 (1H, d, J = 2.0 Hz), 6.51 (1H, dd, J = 8.5, 1.9 Hz), 6.71 (1H, d, J = 1.2 Hz), 7.00 (1H, dd, J = 9.8, 2.3 Hz), 7.15 (1H, d, J = 8.5 Hz), 7.29 (1H, s), 7.43 (1H, d, J = 9.8 Hz), 7.85 (1H, d, J = 2.3 Hz)
6658	1.57 (2H, dd, J = 4.5, 1.7 Hz), 1.83 (2H, dd, J = 4.6, 1.7 Hz), 2.42 (3H, s), 3.56 (2H, d, J = 6.1 Hz), 3.73 (2H, s), 4.32 (2H, s), 5.94 (1H, t, J = 6.1 Hz), 6.63 - 6.67 (1H, m), 6.87 (1H, d, J = 8.6 Hz), 6.99 (1H, dd, J = 9.7, 2.3 Hz), 7.29 (1H, s), 7.38 - 7.47 (3H, m), 7.84 (1H, d, J = 2.3 Hz)

Example No	NMR write-up
6659	1.56 (2H, dd, J = 4.5, 1.7 Hz), 1.80 (2H, dd, J = 4.5, 1.7 Hz), 2.41 (3H, s), 3.45 (2H, d, J = 6.1 Hz), 3.58 (2H, q, J = 11.4 Hz), 3.73 (2H, s), 4.31 (2H, s), 5.35 (1H, t, J = 6.1 Hz), 6.54 - 6.59 (1H, m), 6.68 (1H, dd, J = 8.3, 1.2 Hz), 6.97 (1H, dd, J = 9.7, 2.3 Hz), 7.07 (1H, d, J = 7.2 Hz), 7.09 - 7.14 (1H, m), 7.29 (1H, d, J = 1.0 Hz), 7.43 (1H, dd, J = 9.7, 0.8 Hz), 7.83 (1H, d, J = 2.4 Hz)
6660	1.57 (2H, dd, J = 4.5, 1.7 Hz), 1.84 (2H, d, J = 4.5 Hz), 2.42 (3H, d, J = 0.9 Hz), 3.73 (2H, s), 4.33 (2H, s), 5.26 (2H, s), 5.60 (1H, d, J = 2.1 Hz), 5.89 (1H, dd, J = 5.9, 2.1 Hz), 6.06 (1H, t, J = 6.0 Hz), 7.00 (1H, dd, J = 9.7, 2.4 Hz), 7.29 (1H, d, J = 1.0 Hz), 7.41 - 7.46 (2H, m), 7.83 - 7.87 (1H, m)
6661	1.59 (2H, dd, J = 4.4, 1.7 Hz), 1.86 (2H, dd, J = 4.5, 1.7 Hz), 2.42 (3H, s), 3.39 (2H, d, J = 6.0 Hz), 3.74 (2H, s), 4.33 (2H, s), 5.87 (1H, t, J = 6.0 Hz), 6.94 - 7.02 (2H, m), 7.05 (1H, dd, J = 8.3, 4.5 Hz), 7.29 (1H, s), 7.44 (1H, d, J = 9.7 Hz), 7.74 (1H, dd, J = 4.5, 1.4 Hz), 7.85 (1H, d, J = 2.4 Hz), 8.03 (1H, d, J = 2.9 Hz)
6663	1.50 - 1.57 (2H, m), 1.78 - 1.84 (2H, m), 2.42 (3H, s), 3.60 (2H, d, J = 5.8 Hz), 3.69 - 3.73 (5H, m), 4.32 (2H, s), 6.08 (1H, d, J = 2.3 Hz), 6.12 (1H, dd, J = 5.8, 2.2 Hz), 6.36 (1H, t, J = 5.9 Hz), 7.00 (1H, dd, J = 9.7, 2.3 Hz), 7.29 (1H, s), 7.43 (1H, d, J = 9.7 Hz), 7.76 (1H, d, J = 5.8 Hz), 7.84 (1H, d, J = 2.3 Hz)
7702	1.37 (6H, s), 1.95 - 2.05 (4H, m), 4.27 (2H, s), 4.28 (2H, s), 6.62 (1H, dd, J = 7.4, 2.5 Hz), 6.72 (2H, s), 7.04 (1H, d, J = 2.5 Hz), 7.08 - 7.12 (1H, m), 7.12 - 7.15 (1H, m), 7.35 (1H, t, J = 8.1 Hz), 7.39 (1H, d, J = 1.3 Hz), 7.73 (1H, d, J = 8.4 Hz), 7.75 (1H, d, J = 1.1 Hz), 7.81 (1H, d, J = 5.9 Hz), 8.33 - 8.44 (1H, m)
7703	1.33 (6H, s), 1.82 - 1.89 (4H, m), 3.47 (2H, d, J = 5.7 Hz), 4.10 (2H, s), 5.90 (1H, t, J = 6.0 Hz), 6.51 (2H, s), 6.67 (1H, d, J = 7.7 Hz), 6.71 (1H, s), 7.00 (1H, dd, J = 9.7, 2.3 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.4 Hz), 7.43 (1H, d, J = 9.7 Hz), 7.48 (1H, d, J = 1.1 Hz) 7.73 (1H, t, J = 6.2 Hz), 7.79 - 7.83 (1H, m), 8.29 (1H, d, J = 2.0 Hz)
7704	1.37 (6H, s), 1.99 - 2.04 (4H, m), 4.19 (2H, s), 4.29 (2H, s), 6.71 (2H, s), 7.05 (1H, dd, J = 9.7, 2.2 Hz), 7.11 (2H, d, J = 6.6 Hz), 7.35 (1H, t, J = 8.1 Hz), 7.48 (1H, d, J = 9.8 Hz), 7.51 (1H, s), 7.73 (1H, t, J = 8.3 Hz), 7.81 (1H, d, J = 5.9 Hz), 7.83 (1H, s), 8.35 (1H, d, J = 1.8 Hz)
8801	2.12 - 2.23 (2H, m), 2.52 - 2.59 (2H, m), 3.97 - 4.07 (5H, m), 4.43 (2H, d, J = 1.0 Hz), 6.57 (1H, d, J = 7.6 Hz), 6.61 (2H, s), 6.82 - 6.88 (2H, m), 7.26 (1H, t, J = 8.0 Hz), 7.47 - 7.49 (1H, m), 7.51 - 7.57 (2H, m), 7.67 (1H, d, J = 6.1 Hz), 7.92 (1H, t, J = 1.0 Hz), 8.51 (1H, dd, J = 6.9, 1.0 Hz)

Example No	NMR write-up
8803	1.90 - 2.06 (4H, m), 2.26 - 2.38 (2H, m), 3.25 - 3.37 (4H, m), 4.03 - 4.19 (1H, m), 4.42 (2H, d, J = 6.0 Hz), 6.55 (2H, d, J = 5.3 Hz), 6.80 - 6.86 (1H, m), 6.95 (1H, dd, J = 16.7, 7.7 Hz), 7.05 (1H, d, J = 6.1 Hz), 7.27 (1H, td, J = 8.0, 3.9 Hz), 7.47 (1H, s), 7.53 (1H, d, J = 0.9 Hz), 7.62 (1H, dd, J = 11.7, 8.2 Hz), 7.70 (1H, dd, J = 6.1, 4.2 Hz), 7.90 (1H, s), 8.49 (1H, dd, J = 6.9, 3.0 Hz)
8804	1.96 - 2.05 (4H, m), 2.31 - 2.38 (2H, m), 3.25 - 3.34 (4H, m), 4.09 (1H, p, J = 7.0 Hz), 4.42 (2H, s), 6.56 (2H, s), 6.84 (1H, dd, J = 7.0, 1.6 Hz), 6.97 (1H, d, J = 7.6 Hz), 7.05 (1H, d, J = 6.2 Hz), 7.27 (1H, t, J = 8.0 Hz), 7.47 (1H, s), 7.53 (1H, d, J = 1.2 Hz), 7.63 (1H, d, J = 8.2 Hz), 7.70 (1H, d, J = 6.1 Hz), 7.90 (1H, s), 8.49 (1H, dd, J = 6.9, 1.0 Hz). Signals at 3.3 ppm overlap with water peak.
8805	1.95 (2H, t, J = 6.6 Hz), 1.98 - 2.05 (2H, m), 2.26 - 2.34 (2H, m), 3.28 - 3.38 (4H, m), 4.13 (1H, p, J = 7.0 Hz), 4.43 (2H, s), 6.55 (2H, s), 6.83 (1H, dd, J = 7.0, 1.7 Hz), 6.94 (1H, d, J = 7.7 Hz), 7.05 (1H, d, J = 6.2 Hz), 7.26 (1H, t, J = 8.0 Hz), 7.47 (1H, s), 7.53 (1H, d, J = 1.2 Hz), 7.61 (1H, d, J = 8.3 Hz), 7.69 (1H, d, J = 6.1 Hz), 7.90 (1H, s), 8.49 (1H, d, J = 6.8 Hz). Signals at 3.3 ppm overlap with water peak.
8806	(CD_3OD) 2.09 (4H, td, J = 7.4, 3.9 Hz), 2.29 - 2.37 (2H, m), 2.82 (1H, tt, J = 8.5, 6.3 Hz), 3.42 (2H, t, J= 6.8 Hz), 3.51 (2H, s), 4.09 (2H, d, J = 6.4 Hz), 6.66 (1H, dd, J = 7.4, 2.4 Hz), 6.88 (1H, d, J = 2.5 Hz), 7.15 (1H, dd, J = 7.8,0.9 Hz), 7.31 (1H, dd, J = 6.3, 1.0 Hz), 7.36 - 7.44 (2H, m), 7.62 (1H, dt, J = 8.4, 1.0 Hz), 7.66 (1H, dd, J = 1.5, 0.7 Hz), 7.71(1H, d, J = 6.3 Hz), 8.28 (1H, dd, J = 7.4, 0.7 Hz)
8807	(CD_3OD) 2.05 - 2.14 (2H, m), 2.18 (2H, t, J = 6.6 Hz), 2.22 - 2.30 (2H, m), 2.87 (1H, tt, J = 8.3, 6.1 Hz),3.43 (2H, s), 3.48 (2H, q, J = 7.2 Hz), 4.05 (2H, d, J = 6.2 Hz), 6.59 - 6.69 (1H, m), 6.85 (1H, d, J = 2.5 Hz), 7.11 (1H, dd, J =7.8, 0.9 Hz), 7.29 (1H, dd, J = 6.4, 1.0 Hz), 7.34 - 7.49 (2H, m), 7.59 (1H, dt, J = 8.4, 1.0 Hz), 7.61 - 7.73 (2H, m), 8.22 -8.31 (1H, m)
8808	2.07 - 2.18 (2H, m), 2.37 - 2.47 (2H, m), 2.59 - 2.73 (1H, m), 3.95 (2H, d, J = 6.5 Hz), 4.07 (4H, d, J = 23.8 Hz), 6.56 (2H, s), 6.59 (1H, d, J = 7.6 Hz), 6.89 (1H, dd, J = 6.2, 0.9 Hz), 7.03 (1H, dd, J = 9.7, 2.4 Hz), 7.27 (1H, t, J = 7.9 Hz), 7.47 (1H, d, J = 9.7 Hz), 7.50 (1H, d, J = 1.1 Hz), 7.54 (1H, d, J = 8.3 Hz), 7.68 (1H, d, J = 6.1 Hz), 7.83 (1H, t, J = 0.9 Hz), 8.28 (1H, dd, J = 2.4, 0.8 Hz)

Example No	NMR write-up
9001	1.66 - 1.81 (2H, m), 1.90 - 1.99 (1H, m), 2.07 - 2.15 (1H, m), 3.94 (2H, dd, J = 15.2, 7.7 Hz), 4.00 - 4.09 (2H, m), 4.49 (1H, d, J = 7.3 Hz), 4.56 - 4.68 (2H, m), 6.57 (2H, s), 6.62 (1H, d, J = 7.7 Hz), 6.83 (1H, dd, J = 7.0, 1.7 Hz), 6.87 (1H, d, J = 6.1 Hz), 7.27 (1H, t, J = 7.9 Hz), 7.48 (1H, d, J = 1.6 Hz), 7.52 (1H, d, J = 1.2 Hz), 7.54 (1H, d, J = 8.3 Hz), 7.66 (1H, d, J = 6.1 Hz), 7.87 (1H, t, J = 1.0 Hz), 8.43 (1H, dd, J = 7.0, 0.9 Hz)
9002	1.68 - 1.81 (2H, m), 1.90 - 1.99 (1H, m), 2.06 - 2.16 (1H, m), 3.88 - 4.00 (2H, m), 4.00 - 4.12 (2H, m), 4.49 (1H, d, J = 7.4 Hz), 4.55 - 4.71 (2H, m), 6.56 (2H, s), 6.61 (1H, d, J = 7.7 Hz), 6.83 (1H, dd, J = 7.0, 1.6 Hz), 6.87 (1H, d, J = 6.1 Hz), 7.27 (1H, t, J = 7.9 Hz), 7.48 (1H, s), 7.50 - 7.57 (2H, m), 7.66 (1H, d, J = 6.0 Hz), 7.87 (1H, s), 8.43 (1H, d, J = 7.3 Hz).
9003	1.67 - 1.82 (2H, m), 1.90 - 1.98 (1H, m), 2.07 - 2.15 (1H, m), 3.88 - 3.98 (2H, m), 4.00 - 4.09 (2H, m), 4.49 (1H, d, J = 7.4 Hz), 4.56 - 4.68 (2H, m), 6.56 (2H, s), 6.61 (1H, d, J = 7.6 Hz), 6.83 (1H, dd, J = 7.0, 1.7 Hz), 6.87 (1H, d, J = 6.1 Hz), 7.27 (1H, t, J = 8.0 Hz), 7.48 (1H, s), 7.50 - 7.57 (2H, m), 7.66 (1H, d, J = 6.1 Hz), 7.87 (1H, s), 8.43 (1H, d, J = 6.9 Hz).
10901	2.03 (2H, dd, J = 8.5, 6.1 Hz), 2.07 - 2.12 (2H, m), 2.15 (2H, t, J = 6.9 Hz), 3.32 (2H, s), 3.86 (2H, s), 4.26 (2H, t, J = 6.9 Hz), 4.65 (1H, s), 5.40 (2H, s), 6.51 (1H, dd, J = 7.4, 2.5 Hz), 6.74 (1H, d, J = 7.8 Hz), 6.84 (1H, d, J = 2.4 Hz), 7.00 (1H, dd, J = 6.3, 1.0 Hz), 7.14 (1H, d, J = 8.3 Hz), 7.36 (1H, t, J = 8.0 Hz), 7.41 (1H, d, J = 1.2 Hz), 7.48 (1H, d, J = 1.4 Hz), 7.86 - 7.97 (2H, m)
10903	1.66 - 1.73 (2H, m), 1.80 (2H, t, J = 8.5 Hz), 1.87 (2H, t, J = 6.9 Hz), 1.94 - 2.01 (2H, m), 2.69 (1H, dd, J = 16.6, 5.3 Hz), 2.92 (1H, dd, J = 16.6, 4.5 Hz), 3.18 (2H, d, J = 5.8 Hz), 3.30 (2H, d, J = 2.0 Hz), 3.79 - 3.88 (3H, m), 4.02 (2H, t, J = 6.8 Hz), 5.68 (1H, t, J = 6.0 Hz), 6.50 (2H, s), 6.60 (1H, d, J = 7.7 Hz), 6.76 (1H, d, J = 1.2 Hz), 6.92 (1H, d, J = 1.2 Hz), 7.07 (1H, d, J = 6.1 Hz), 7.19 (1H, t, J = 8.0 Hz), 7.32 (1H, d, J = 8.3 Hz), 7.72 (1H, d, J = 6.0 Hz)
10904	1.82 - 1.90 (2H, m), 1.97 (2H, d, J = 8.0 Hz), 2.04 (2H, t, J = 6.8 Hz), 3.24 (2H, d, J = 5.8 Hz), 3.79 (2H, s), 4.10 (2H, t, J = 6.8 Hz), 5.75 (1H, t, J = 6.0 Hz), 6.50 (2H, s), 6.65 (1H, d, J = 7.7 Hz), 6.94 (1H, dd, J = 9.7, 2.4 Hz), 7.09 - 7.14 (1H, m), 7.21 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.42 (1H, dd, J = 9.7, 0.9 Hz), 7.47 (1H, d, J = 1.1 Hz), 7.73 (1H, d, J = 6.1 Hz), 7.77 (1H, t, J = 0.9 Hz), 8.22 (1H, dd, J = 2.4, 0.8 Hz)
10906	1.81 (2H, td, J = 6.7, 1.5 Hz), 1.88 - 1.95 (2H, m), 1.95 - 2.01 (2H, m), 3.22 (2H, d, J = 5.6 Hz), 3.30 (3H, s, in water peak), 3.77 (2H, s), 4.07 (2H, t, J = 6.8 Hz), 5.74 (1H, d, J = 2.7 Hz), 5.74 - 5.79 (1H, m), 5.83 (1H, dd, J = 7.5, 2.7 Hz), 6.59 - 6.70 (3H, m), 7.09 - 7.14 (1H, m), 7.22 (1H, t, J = 8.0 Hz), 7.35 (1H, d, J = 8.3 Hz), 7.51 (1H, d, J = 7.5 Hz), 7.72 (1H, d, J = 6.2 Hz)

Example No	NMR write-up
10907	1.80 (2H, dd, J = 7.0, 2.5 Hz), 1.95 (2H, d, J = 7.8 Hz), 2.02 (2H, t, J = 6.8 Hz), 2.30 (3H, d, J = 1.0 Hz), 3.25 (2H, d, J = 6.2 Hz), 3.86 (2H, s), 4.07 (2H, t, J = 6.8 Hz), 6.09 (1H, d, J = 5.6 Hz), 6.14 (1H, t, J = 6.2 Hz), 6.25 (1H, dd, J = 2.1, 1.1 Hz), 6.51 (1H, dd, J = 7.4, 2.5 Hz), 6.87 (1H, d, J = 2.5 Hz), 7.35 (1H, d, J = 1.3 Hz), 7.68 (1H, d, J = 5.5 Hz), 7.71 (1H, dd, J = 1.3, 0.7 Hz), 8.34 (1H, dd, J = 7.4, 0.7 Hz), 10.91 (1H, s)
10908	1.68 - 1.90 (7H, m), 1.96 - 2.03 (1H, m), 2.58 - 2.72 (2H, m), 3.18 (2H, d, J = 5.7 Hz), 3.28 - 3.36 (2H, m), 3.82 - 3.88 (2H, m), 3.97 - 4.03 (3H, m), 5.69 (1H, t, J = 5.9 Hz), 6.50 (2H, s), 6.60 (1H, d, J = 7.7 Hz), 6.76 (1H, d, J = 0.9 Hz), 6.88 (1H, d, J = 1.2 Hz), 7.07 (1H, d, J = 6.1 Hz), 7.19 (1H, t, J = 8.0 Hz), 7.32 (1H, d, J = 8.3 Hz), 7.73 (1H, d, J = 6.1 Hz)
10909	1H NMR (CD3CN) δ 1.82 (2H, dd, J = 7.2, 2.4 Hz), 1.89 - 1.92 (2H, m), 2.00 (2H, t, J = 6.8 Hz), 3.26 (2H, d, J = 6.0 Hz), 3.71 (2H, s), 4.05 (2H, t, J = 6.8 Hz), 4.99 (1H, s), 5.16 (1H, t, J = 5.8 Hz), 6.19 (1H, t, J = 6.0 Hz), 6.35 (1H, s), 6.86 (1H, dd, J = 9.8, 2.3 Hz), 7.31 (1H, d, J = 9.7 Hz), 7.38 (1H, d, J = 0.8 Hz), 7.55 (1H, s), 7.77 (1H, J = 5.7 Hz), 7.82 (1H, d, J = 2.0 Hz)
10910	1.84 - 1.91 (2H, m), 1.98 (2H, t, J = 7.2 Hz), 2.05 (2H, t, J = 6.8 Hz), 3.24 (2H, d, J = 5.7 Hz), 4.09 (2H, t, J = 6.8 Hz), 4.21 (2H, s), 5.72 (1H, t, J = 5.9 Hz), 6.52 (2H, s), 6.64 (1H, d, J = 7.7 Hz), 7.08 - 7.11 (1H, m), 7.13 (1H, d, J = 9.9 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.57 (1H, t, J = 51.5 Hz), 7.73 (1H, d, J = 6.0 Hz), 8.35 (1H, d, J = 9.9 Hz)
10911	1.78 - 1.87 (2H, m), 1.88 - 1.96 (2H, m), 2.01 (2H, t, J = 6.9 Hz), 3.22 (2H, d, J = 5.7 Hz), 3.40 (3H, s), 3.72 (2H, s), 4.08 (2H, t, J = 6.8 Hz), 5.72 (1H, t, J = 5.9 Hz), 6.04 (1H, t, J = 7.1 Hz), 6.51 (2H, s), 6.63 (1H, d, J = 7.7 Hz), 6.78 (1H, dd, J = 7.5, 1.8 Hz), 7.10 (1H, d, J = 6.2 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.24 (1H, dd, J = 6.9, 1.7 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.72 (1H, d, J = 6.1 Hz)
10912	1.81 - 1.86 (2H, m), 1.90 - 1.97 (2H, m), 2.01 (2H, t, J = 6.8 Hz), 3.23 (2H, d, J = 5.7 Hz), 4.08 (2H, t, J = 6.6 Hz), 4.16 (2H, s), 5.71 (1H, t, J = 5.8 Hz), 6.50 (2H, s), 6.63 (1H, d, J = 7.7 Hz), 7.08 - 7.11 (2H, m), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.2 Hz), 7.72 (1H, d, J = 6.1 Hz), 8.55 (2H, d, J = 4.6 Hz)
10914	1.78 - 1.85 (2H, m), 1.88 - 1.97 (2H, m), 1.97 - 2.04 (2H, m), 3.23 (2H, d, J = 5.8 Hz), 4.08 (2H, t, J = 6.8 Hz), 4.11 (2H, s), 5.72 (1H, t, J = 6.0 Hz), 6.61 (2H, s), 6.66 (1H, d, J = 7.8 Hz), 6.72 (1H, dd, J = 8.3, 1.0 Hz), 6.93 (1H, ddd, J = 7.1, 5.0, 1.0 Hz), 7.11 (1H, d, J = 6.1 Hz), 7.22 (1H, t, J = 8.0 Hz), 7.35 (1H, d, J = 8.3 Hz), 7.61 - 7.69 (1H, m), 7.72 (1H, d, J = 6.1 Hz), 8.10 (1H, ddd, J = 5.0, 2.0, 0.8 Hz)

Example No	NMR write-up
10915	1.73 - 1.82 (4H, m), 1.84 (2H, t, J = 6.9 Hz), 3.14 (2H, d, J = 5.8 Hz), 3.89 (2H, s), 4.00 (2H, t, J = 6.8 Hz), 5.61 (1H, t, J = 5.9 Hz), 6.11 (1H, td, J = 6.6, 1.4 Hz), 6.33 (1H, dd, J = 9.3, 1.3 Hz), 6.49 (2H, s), 6.59 (1H, d, J = 7.7 Hz), 7.03 (1H, d, J = 6.1 Hz), 7.18 (1H, t, J = 8.0 Hz), 7.33 (2H, ddt, J = 8.9, 4.0, 2.1 Hz), 7.46 (1H, dd, J = 6.8, 2.1 Hz), 7.71 (1H, d, J = 6.1 Hz)
10918	($CDCl_3$) 1.90 - 2.04 (4H, m), 2.11 (2H, t, J = 6.9 Hz), 3.15 (2H, s), 3.86 (2H, s), 3.97 (1H, s), 4.16 - 4.22 (2H, m), 6.56 (3H, ddd, J = 12.8, 8.1, 1.7 Hz), 6.93 (1H, d, J = 2.4 Hz), 7.07 - 7.14 (2H, m), 7.42 (1H, s), 7.50 (1H, s), 7.96 (1H, d, J = 7.4 Hz)
10919	($CDCl_3$) 1.91 - 2.05 (4H, m), 2.11 (2H, t, J = 6.9 Hz), 3.17 (2H, d, J = 5.0 Hz), 3.88 (2H, s), 4.05 (1H, d, J = 6.0 Hz), 4.19 (2H, t, J = 6.9 Hz), 6.50 (1H, ddd, J = 8.2, 2.3, 0.9 Hz), 6.58 - 6.65 (2H, m), 6.65 (1H, ddd, J = 7.9, 2.0, 0.9 Hz), 7.00 (1H, d, J = 2.4 Hz), 7.05 (1H, t, J = 8.0 Hz), 7.41 - 7.45 (1H, m), 7.51 (1H, d, J = 1.6 Hz), 7.98 (1H, d, J = 7.4 Hz)
10920	1.76 - 1.83 (2H, m), 1.88 (3H, d, J = 1.1 Hz), 1.99 - 2.14 (4H, m), 3.25 (2H, d, J = 5.9 Hz), 3.83 (2H, s), 4.11 (2H, t, J = 6.8 Hz), 5.88 (1H, t, J = 6.1 Hz), 6.49 (2H, s), 6.62 (1H, d, J = 7.7 Hz), 6.80 (1H, s), 7.12 (1H, d, J = 6.1 Hz), 7.19 (1H, t, J = 8.0 Hz), 7.26 - 7.34 (2H, m), 7.59 (1H, d, J = 1.2 Hz), 7.73 (1H, d, J = 6.1 Hz), 8.18 (1H, d, J = 1.4 Hz)
10921	1.80 - 1.88 (2H, m), 1.93 - 2.06 (4H, m), 3.36 (2H, d, J = 6.1 Hz), 3.87 (2H, s), 4.07 (2H, t, J = 6.8 Hz), 6.48 (1H, dd, J = 7.4, 2.5 Hz), 6.54 (1H, d, J = 5.5 Hz), 6.86 (1H, d, J = 2.5 Hz), 7.28 (1H, t, J = 6.3 Hz), 7.35 (1H, d, J = 1.3 Hz), 7.45 (1H, dd, J = 9.0, 2.3 Hz), 7.71 (1H, t, J = 1.0 Hz), 7.78 (1H, d, J = 2.3 Hz), 8.29 - 8.37 (2H, m), 8.37 (1H, d, J = 5.4 Hz)
10922	(CD_3OD) 1.99 - 2.14 (4H, m), 2.15 - 2.22 (2H, m), 3.41 (2H, s), 4.03 (2H, s), 4.21 - 4.27 (2H, m), 4.62 (2H, s), 6.80 - 6.93 (1H, m), 7.02 (2H, dd, J = 15.1, 2.4 Hz), 7.15 - 7.26 (1H, m), 7.56 - 7.63 (2H, m), 7.79 (1H, d, J = 1.8 Hz), 8.07 (1H, d, J = 9.2 Hz), 8.38 - 8.44 (1H, m)
10923	1.80 (2H, dd, J = 7.1, 2.5 Hz), 2.04 (4H, d, J = 8.1 Hz), 2.13 (3H, s), 3.24 (2H, d, J = 5.7 Hz), 3.88 (2H, s), 4.11 (2H, t, J = 6.8 Hz), 5.85 (1H, t, J = 6.1 Hz), 6.49 (2H, s), 6.62 (1H, d, J = 7.7 Hz), 6.82 (1H, d, J = 7.5 Hz), 7.12 (1H, d, J = 6.1 Hz), 7.19 (1H, t, J = 8.0 Hz), 7.32 (1H, d, J = 8.3 Hz), 7.38 (1H, d, J = 1.3 Hz), 7.69 - 7.75 (2H, m), 8.32 (1H, d, J = 7.4 Hz)
10924	1.79 - 1.87 (2H, m), 1.96 (2H, d, J = 8.1 Hz), 2.04 (2H, t, J = 6.9 Hz), 3.24 (2H, d, J = 5.8 Hz), 3.81 (2H, s), 4.10 (2H, t, J = 6.8 Hz), 5.75 (1H, t, J = 6.0 Hz), 6.51 (2H, s), 6.64 (1H, d, J = 7.7 Hz), 7.11 (1H, d, J = 6.1 Hz), 7.22 (1H, s), 7.24 (1H, d, J = 2.1 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.54 (1H, d, J = 1.1 Hz), 7.73 (1H, d, J = 6.0 Hz), 7.89 (1H, d, J = 1.1 Hz), 8.28 (1H, d, J = 2.1 Hz)

Example No	NMR write-up
10925	1.83 (2H, dd, J = 7.0, 2.5 Hz), 1.97 (2H, dt, J = 8.5, 4.2 Hz), 2.03 (2H, t, J = 6.9 Hz), 2.50 (3H, d, J = 1.6 Hz), 3.24 (2H, d, J = 5.8 Hz), 3.86 (2H, s), 4.10 (2H, t, J = 6.8 Hz), 5.75 (1H, t, J = 6.0 Hz), 6.41 (1H, dd, J = 2.5, 1.1 Hz), 6.50 (2H, s), 6.65 (1H, d, J = 7.7 Hz), 6.79 (1H, d, J = 2.4 Hz), 7.11 (1H, d, J = 6.1 Hz), 7.16 - 7.26 (1H, m), 7.33 (1H, d, J = 8.3 Hz), 7.42 (1H, d, J = 1.3 Hz), 7.56 - 7.64 (1H, m), 7.74 (1H, d, J = 6.1 Hz)
10926	1.85 (2H, dd, J = 7.1, 2.1 Hz), 1.97 (2H, d, J = 8.8 Hz), 2.04 (2H, t, J = 6.8 Hz), 3.24 (2H, d, J = 5.7 Hz), 3.93 (2H, s), 4.10 (2H, t, J = 6.8 Hz), 5.78 (1H, t, J = 5.8 Hz), 6.52 (2H, s), 6.59 (1H, dd, J = 7.4, 2.2 Hz), 6.64 (1H, d, J = 7.7 Hz), 7.02 (1H, d, J = 2.2 Hz), 7.11 (1H, d, J = 6.1 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.73 (1H, d, J = 6.1 Hz), 8.38 (1H, d, J = 7.5 Hz), 8.45 (1H, s)
10928	1.75 - 1.86 (2H, m), 1.91 (2H, dt, J = 8.4, 4.2 Hz), 1.96 (2H, t, J = 6.9 Hz), 2.25 (3H, s), 3.22 (2H, d, J = 5.9 Hz), 3.29 (3H, s), 3.74 (2H, s), 4.06 (2H, t, J = 6.8 Hz), 5.64 (1H, d, J = 2.8 Hz), 5.73 - 5.81 (2H, m), 6.64 - 6.71 (3H, m), 7.13 (1H, d, J = 6.3 Hz), 7.23 (1H, t, J = 8.0 Hz), 7.35 (1H, d, J = 8.3 Hz), 7.71 (1H, d, J = 6.2 Hz)
10929	1.81 - 1.90 (2H, m), 1.96 (2H, dt, J = 8.3, 4.1 Hz), 2.04 (2H, t, J = 6.8 Hz), 3.25 (2H, d, J = 5.8 Hz), 3.81 (2H, s), 4.10 (2H, t, J = 6.8 Hz), 5.82 (1H, t, J = 6.0 Hz), 6.68 (3H, d, J = 8.8 Hz), 7.09 (1H, dd, J = 9.9, 2.2 Hz), 7.14 (1H, d, J = 6.3 Hz), 7.23 (1H, t, J = 8.0 Hz), 7.36 (1H, d, J = 8.3 Hz), 7.67 (1H, d, J = 9.8 Hz), 7.72 (1H, d, J = 6.2 Hz), 8.20 (1H, d, J = 2.2 Hz), 9.05 (1H, s)
10930	1.84 (2H, dd, J = 7.1, 2.2 Hz), 1.98 (2H, d, J = 8.8 Hz), 2.04 (2H, t, J = 6.9 Hz), 2.37 (3H, s), 3.24 (2H, d, J = 4.8 Hz), 3.87 (2H, s), 4.10 (2H, t, J = 6.8 Hz), 5.76 (1H,s), 6.54 (1H, dd, J = 7.5, 2.4 Hz), 6.57 (2H, s), 6.65 (1H, d, J = 7.7 Hz), 6.84 (1H, d, J = 2.3 Hz), 7.11 (1H, d, J = 6.3 Hz), 7.13 (1H, s), 7.21 (1H, t, J = 8.0 Hz), 7.34 (1H, d, J = 8.3 Hz), 7.73 (1H, d, J = 6.1 Hz), 8.06 (1H, d, J = 7.4 Hz), 8.19 (2H, s)
10931	1.78 - 1.88 (2H, m), 1.93 - 2.00 (2H, m), 2.03 (2H, t, J = 6.9 Hz), 3.24 (2H, d, J = 5.8 Hz), 3.87 (2H, s), 4.09 (2H, t, J = 6.8 Hz), 4.26 (2H, s), 5.76 (1H, t, J = 6.0 Hz), 6.52 (2H, s), 6.64 (1H, d, J = 7.7 Hz), 6.94 (1H, dd, J = 8.4, 2.2 Hz), 7.03 (1H, d, J = 2.2 Hz), 7.11 (1H, d, J = 6.1 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.51 (1H, d, J = 8.4 Hz), 7.73 (1H, d, J = 6.1 Hz), 8.30 (1H, s)
10932	(CD_3CN) 1.92 - 2.08 (8H, m), 2.12 (2H, t, J = 6.9 Hz), 4.17 (2H, dt, J = 16.4, 6.9 Hz), 4.91 (1H, t, J = 5.9 Hz), 5.56 (2H, s), 6.62 (1H, dd, J = 7.5, 2.5 Hz), 6.76 (1H, d, J = 7.7 Hz), 6.87 (1H, d, J = 2.5 Hz), 7.04 (1H, dd, J = 6.2, 1.0 Hz), 7.17 - 7.25 (1H, m), 7.34 (1H, t, J = 8.0 Hz), 7.84 (1H, dd, J = 6.1, 3.7 Hz), 7.97 (1H, t, J = 1.1 Hz), 8.15 (1H, d, J = 7.5 Hz)

Example No	NMR write-up
10933	1.76 (2H, dd, J = 7.1, 2.6 Hz), 1.98 (2H, t, J = 6.9 Hz), 2.03 (2H, d, J = 7.8 Hz), 3.22 (2H, d, J = 5.9 Hz), 3.29 (3H, s), 3.82 (2H, s), 4.08 (2H, t, J = 6.8 Hz), 5.85 (2H, d, J = 8.9 Hz), 6.46 (2H, s), 6.59 (1H, d, J = 7.8 Hz), 7.10 (1H, d, J = 6.2 Hz), 7.18 (1H, t, J = 8.0 Hz), 7.31 (1H, d, J = 8.3 Hz), 7.71 (1H, d, J = 6.1 Hz), 7.87 (1H, s)
10934	(CD_3OD) δ 1.36 (6H, d, J = 6.8 Hz), 1.97 - 2.08 (4H, m), 2.13 (2H, t, J = 6.9 Hz), 3.35 (2H, s), 3.87 (2H, s), 4.24 (2H, t, J = 6.9 Hz), 5.11 (1H, hept, J = 6.8 Hz), 5.91 (1H, d, J = 2.8 Hz), 6.12 (1H, dd, J = 7.8, 2.7 Hz), 6.83 (1H, dd, J = 6.6, 2.2 Hz), 7.11 (1H, dd, J = 6.3, 0.8 Hz), 7.32 - 7.40 (2H, m), 7.56 (1H, d, J = 7.7 Hz), 7.73 (1H, d, J = 6.3 Hz)
10936	1.83 (2H, dd, J = 7.1, 2.5 Hz), 1.93 (2H, dt, J = 8.4, 4.2 Hz), 1.99 (2H, t, J = 6.9 Hz), 3.22 (2H, d, J = 5.8 Hz), 4.04 (2H, s), 4.07 (2H, t, J = 6.8 Hz), 5.69 (1H, t, J = 5.9 Hz), 6.28 (1H, d, J = 1.8 Hz), 6.49 (2H, s), 6.63 (1H, dd, J = 7.8, 0.8 Hz), 7.09 (1H, dd, J = 6.3, 0.8 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.72 (1H, d, J = 6.1 Hz), 8.63 (1H, d, J = 1.8 Hz)
10937	1.78 - 1.86 (2H, m), 1.92 (2H, dt, J = 7.8, 3.9 Hz), 1.99 (2H, t, J = 6.8 Hz), 3.22 (2H, d, J = 5.8 Hz), 4.07 (2H, t, J = 6.8 Hz), 4.21 (2H, s), 5.69 (1H, t, J = 6.0 Hz), 6.51 (2H, s), 6.63 (1H, d, J = 7.7 Hz), 6.86 (1H, dd, J = 5.9, 1.2 Hz), 7.08 (1H, d, J = 6.1 Hz), 7.19 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.73 (1H, d, J = 6.1 Hz), 8.47 (1H, d, J = 5.8 Hz), 8.72 (1H, d, J = 1.2 Hz)
10938	1.82 (2H, dd, J = 7.0, 2.5 Hz), 1.89 - 1.98 (2H, m), 2.01 (2H, t, J = 6.8 Hz), 2.81 (2H, t, J = 6.5 Hz), 3.23 (2H, d, J = 5.9 Hz), 3.28 - 3.32 (2H, m), 3.85 (2H, s), 4.09 (2H, t, J = 6.8 Hz), 5.76 (1H, t, J = 5.9 Hz), 6.51 (2H, s), 6.64 (1H, d, J = 7.7 Hz), 6.75 - 6.84 (2H, m), 7.11 (1H, d, J = 6.1 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.64 - 7.79 (3H, m)
10939	1.82 (2H, dd, J = 7.1, 2.3 Hz), 1.95 (2H, d, J = 8.8 Hz), 2.02 (2H, t, J = 6.8 Hz), 2.88 (2H, d, J = 6.6 Hz), 2.97 (3H, s), 3.24 (2H, d, J = 5.3 Hz), 3.48 (2H, t, J = 6.7 Hz), 3.84 (2H, s), 4.09 (2H, t, J = 6.8 Hz), 5.77 (1H, t, J = 5.6 Hz), 6.58 (2H, s), 6.65 (1H, d, J = 7.8 Hz), 6.75 (1H, d, J = 2.3 Hz), 6.81 (1H, dd, J = 8.6, 2.5 Hz), 7.12 (1H, d, J = 6.2 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.34 (1H, d, J = 8.3 Hz), 7.72 (1H, d, J = 2.2 Hz), 7.74 (1H, d, J = 4.8 Hz)
10940	1.75 - 1.83 (2H, m), 1.90 (2H, dt, J = 8.0, 5.6 Hz), 1.96 (2H, t, J = 6.8 Hz), 3.21 (2H, d, J = 5.8 Hz), 3.30 (3H, s), 4.06 (2H, t, J = 6.8 Hz), 4.11 (2H, s), 5.69 (1H, t, J = 5.9 Hz), 5.85 (1H, d, J = 7.1 Hz), 6.51 (2H, s), 6.63 (1H, d, J = 7.6 Hz), 7.09 (1H, d, J = 6.1 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.72 (1H, d, J = 6.1 Hz), 7.92 (1H, d, J = 7.1 Hz)

Example No	NMR write-up
10941	1.83 (2H, dd, J = 7.1, 2.5 Hz), 1.97 (2H, d, J = 7.7 Hz), 2.03 (2H, t, J = 6.9 Hz), 3.24 (2H, d, J = 5.8 Hz), 3.88 (2H, s), 4.09 (2H, t, J = 6.8 Hz), 4.26 (2H, s), 5.75 (1H, t, J = 6.0 Hz), 6.55 (2H, s), 6.65 (1H, d, J = 7.7 Hz), 7.08 (1H, dd, J = 8.3, 2.5 Hz), 7.10 - 7.14 (2H, m), 7.21 (1H, t, J = 8.0 Hz), 7.34 (1H, d, J = 8.3 Hz), 7.41 (1H, d, J = 8.3 Hz), 7.73 (1H, d, J = 6.1 Hz), 8.52 (1H, s)
10942	1.44 (2H, dd, J = 6.5, 2.5 Hz), 1.58 - 1.82 (8H, m), 3.10 (2H, d, J = 5.8 Hz), 3.67 (2H, s), 5.81 (1H, t, J = 6.0 Hz), 6.46 (2H, d, J = 4.7 Hz), 6.58 (1H, d, J = 7.7 Hz), 6.90 (1H, dd, J = 9.7, 2.4 Hz), 7.14 - 7.23 (2H, m), 7.29 (1H, d, J = 8.3 Hz), 7.40 (1H, d, J = 9.7 Hz), 7.46 (1H, d, J = 1.1 Hz), 7.71 - 7.79 (2H, m), 8.18 (1H, d, J = 2.4 Hz)
10943	1.80 (2H, dd, J = 7.1, 2.4 Hz), 1.89 (2H, dt, J = 8.3, 4.1 Hz), 1.99 (2H, t, J = 6.8 Hz), 3.22 (2H, d, J = 5.8 Hz), 3.33 (3H, s), 3.62 (2H, s), 4.07 (2H, t, J = 6.8 Hz), 5.79 (1H, t, J = 5.9 Hz), 6.29 (1H, d, J = 9.8 Hz), 6.56 (2H, s), 6.63 (1H, d, J = 7.7 Hz), 7.10 (1H, d, J = 6.1 Hz), 7.16 - 7.25 (2H, m), 7.30 - 7.36 (2H, m), 7.72 (1H, d, J = 6.1 Hz)
10944	1.82 (2H, dd, J = 7.1, 2.5 Hz), 1.88 - 1.96 (2H, m), 2.00 (2H, t, J = 6.9 Hz), 3.22 (2H, d, J = 5.8 Hz), 3.78 (3H, s), 3.86 (2H, s), 4.08 (2H, t, J = 6.8 Hz), 5.75 (1H, t, J = 6.0 Hz), 6.27 (1H, d, J = 2.2 Hz), 6.44 - 6.55 (3H, m), 6.63 (1H, d, J = 7.7 Hz), 7.10 (1H, d, J = 6.2 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.72 (1H, d, J = 6.1 Hz), 7.91 (1H, d, J = 5.9 Hz)
10945	1.74 - 1.82 (2H, m), 1.94 - 2.06 (4H, m), 3.06 (3H, s), 3.25 (2H, d, J = 5.9 Hz), 3.87 (2H, s), 4.10 (2H, t, J = 6.8 Hz), 5.64 (1H, dd, J = 7.8, 1.1 Hz), 5.93 (1H, dd, J = 9.0, 1.0 Hz), 5.96 (1H, d, J = 6.1 Hz), 6.60 - 6.70 (3H, m), 7.11 - 7.16 (1H, m), 7.21 (1H, t, J = 8.0 Hz), 7.27 - 7.37 (2H, m), 7.72 (1H, d, J = 6.1 Hz)
10946	1.74 - 1.84 (2H, m), 1.92 - 2.03 (4H, m), 3.23 (2H, d, J = 5.9 Hz), 3.59 (3H, s), 3.96 (2H, s), 4.08 (2H, t, J = 6.8 Hz), 5.79 (1H, t, J = 6.0 Hz), 6.51 (2H, s), 6.63 (1H, d, J = 7.7 Hz), 7.10 (1H, d, J = 6.1 Hz), 7.16 - 7.24 (2H, m), 7.33 (1H, d, J = 8.3 Hz), 7.72 (1H, d, J = 6.1 Hz)
10948	1.18 (6H, d, J = 6.9 Hz), 1.77 - 1.84 (2H, m), 1.88 - 1.96 (2H, m), 1.96 - 2.03 (2H, m), 2.87 (1H, h, J = 6.9 Hz), 3.22 (2H, d, J = 5.7 Hz), 4.07 (2H, t, J = 6.8 Hz), 4.18 (2H, s), 5.70 (1H, t, J = 5.9 Hz), 6.50 (2H, s), 6.63 (1H, d, J = 7.7 Hz), 6.68 (1H, d, J = 1.1 Hz), 7.09 (1H, dd, J = 6.3, 0.9 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.73 (1H, d, J = 6.1 Hz), 8.62 (1H, d, J = 1.1 Hz)

Example No	NMR write-up
10949	1.14 (6H, d, J = 6.7 Hz), 1.80 (2H, dd, J = 7.1, 2.3 Hz), 1.93 (2H, d, J = 8.9 Hz), 1.98 (2H, t, J = 6.8 Hz), 3.00 - 3.09 (1H, m), 3.22 (2H, d, J = 5.8 Hz), 3.36 (3H, s), 3.75 (2H, s), 4.07 (2H, d, J = 6.8 Hz), 5.66 (1H, d, J= 2.6 Hz), 5.69 (1H, d, J= 2.6 Hz), 5.73 (1H, t, J = 5.9 Hz), 6.49 (2H, s), 6.63 (1H, d, J = 7.8 Hz), 7.10 (1H, d, J = 6.2 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.2 Hz), 7.72 (1H, d, J = 6.0 Hz)
10951	1.81 (2H, dd, J = 7.1, 2.3 Hz), 1.94 (2H, d, J = 9.0 Hz), 1.99 (2H, t, J = 6.8 Hz), 3.23 (2H, d, J = 5.8 Hz), 3.40 (3H, s), 3.86 (2H, s), 4.07 (2H, t, J = 6.8 Hz), 5.72 (1H, t, J = 5.9 Hz), 6.09 (1H, d, J = 2.6 Hz), 6.48 (1H, d, J = 2.2 Hz), 6.49 (2H, s), 6.63 (1H, d, J = 7.7 Hz), 7.09 (1H, d, J = 6.1 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.72 (1H, d, J = 6.1 Hz)
10952	1.81 (2H, dd, J = 7.1, 2.4 Hz), 1.92 (2H, dt, J = 8.2, 4.1 Hz), 1.99 (2H, t, J = 6.9 Hz), 3.23 (2H, d, J = 5.8 Hz), 3.77 (2H, s), 4.08 (2H, t, J = 6.8 Hz), 5.64 (1H, d, J = 2.5 Hz), 5.73 (1H, t, J = 6.0 Hz), 5.77 (1H, dd, J = 7.3, 2.5 Hz), 6.50 (2H, s), 6.64 (1H, d, J = 7.7 Hz), 7.10 (1H, d, J = 6.2 Hz), 7.16 - 7.25 (2H, m), 7.33 (1H, d, J = 8.3 Hz), 7.73 (1H, d, J = 6.1 Hz), 11.04 (1H, s)
10953	1.77 - 1.87 (2H, m), 1.88 - 1.98 (2H, m), 2.01 (2H, t, J = 6.8 Hz), 2.36 (3H, s), 3.23 (2H, d, J = 5.9 Hz), 3.86 (2H, s), 4.08 (2H, t, J = 6.8 Hz), 5.77 (1H, t, J = 6.0 Hz), 6.53 (2H, s), 6.63 (1H, d, J = 7.7 Hz), 6.70 (1H, dd, J = 5.8, 2.5 Hz), 6.76 (1H, d, J = 2.5 Hz), 7.11 (1H, d, J = 6.1 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.73 (1H, d, J = 6.1 Hz), 8.18 (1H, d, J = 5.8 Hz)
10954	1.78 - 1.83 (2H, m), 1.93 - 1.99 (2H, m), 2.02 (2H, t, J = 6.8 Hz), 3.22 (2H, d, J = 5.8 Hz), 3.74 (3H, s), 3.86 (2H, s), 4.09 (2H, t, J = 7.0 Hz), 5.79 (1H, t, J = 5.9 Hz), 6.51 (2H, s), 6.61 (1H, d, J = 7.7 Hz), 6.98 (1H, d, J = 5.3 Hz), 7.10 (1H, d, J = 6.1 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.72 (1H, d, J = 6.1 Hz), 8.07 (1H, d J = 5.3 Hz), 8.11 (1H, s)
10955	1.76 - 1.81 (2H, m), 1.90 (2H, d, J = 8.8 Hz), 1.98 (2H, t, J = 6.8 Hz), 2.22 (3H, s), 3.22 (2H, d, J = 5.8 Hz), 4.05 - 4.08 (4H, m), 5.72 (1H, t, J = 5.9 Hz), 6.52 (2H, s), 6.53 (1H, s), 6.63 (1H, d, J = 7.7 Hz), 6.77 (1H, d, J = 4.7 Hz), 7.09 (1H, d, J = 6.1 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.73 (1H, d, J = 6.2 Hz), 7.94 (1H, d, J = 5.2 Hz)
10956	1.75 - 1.84 (2H, m), 1.87 - 1.95 (2H, m), 1.98 (2H, t, J = 6.8 Hz), 2.17 (3H, s), 3.21 (2H, d, J = 5.8 Hz), 4.03 - 4.11 (4H, m), 5.71 (1H, t, J = 6.0 Hz), 6.53 (2H, s), 6.60 - 6.65 (2H, m), 7.09 (1H, dd, J = 6.3, 0.8 Hz), 7.19 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.47 (1H, ddd, J = 8.4, 2.5, 0.7 Hz), 7.73 (1H, d, J = 6.0 Hz), 7.90 (1H, dt, J = 2.5, 0.9 Hz)

Example No	NMR write-up
10957	1.80 (2H, dd, J = 7.1, 2.3 Hz), 1.93 (2H, d, J = 9.1 Hz), 1.99 (2H, t, J = 6.8 Hz), 2.31 (3H, s), 3.22 (2H, d, J = 5.8 Hz), 4.07 (4H, t, J = 6.8 Hz), 5.72 (1H, t, J = 5.9 Hz), 6.50 (1H, s), 6.52 (2H, s), 6.63 (1H, d, J = 7.7 Hz), 6.78 (1H, d, J = 7.1 Hz), 7.09 (1H, d, J = 6.2 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.53 (1H, t, J = 7.7 Hz), 7.72 (1H, d, J = 6.0 Hz)
10958	1.88 (2H, d, J = 7.5 Hz), 1.98 (2H, d, J = 7.7 Hz), 2.05 (2H, q, J = 6.5 Hz), 3.21 (2H, d, J = 5.6 Hz), 3.91 (2H, s), 4.09 (2H, t, J = 6.8 Hz), 6.43 (1H, t, J = 5.8 Hz), 6.57 (1H, d, J = 7.6 Hz), 6.66 (1H, s), 6.89 (1H, s), 7.17 (1H, d, J = 8.8 Hz), 7.34 - 7.41 (2H, m), 7.72 (2H, t, J = 4.6 Hz), 8.16 (1H, d, J = 5.9 Hz), 8.36 (1H, d, J = 7.4 Hz), 8.83 (1H, s)
10961	1.86 (2H, dd, J = 7.0, 2.5 Hz), 1.93 - 2.02 (2H, m), 2.05 (2H, t, J = 6.9 Hz), 3.24 (2H, d, J = 5.8 Hz), 4.00 (2H, s), 4.10 (2H, t, J = 6.8 Hz), 5.75 (1H, t, J = 6.0 Hz), 6.50 (2H, s), 6.64 (1H, d, J = 7.7 Hz), 6.86 (1H, dd, J = 7.5, 2.4 Hz), 7.11 (1H, d, J = 6.2 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.28 - 7.36 (2H, m), 7.73 (1H, d, J = 6.1 Hz), 8.44 (1H, d, J = 7.5 Hz)
10962	1.61 (3H, s), 1.68 - 1.78 (2H, m), 1.95 (4H, t, J = 7.0 Hz), 3.21 (2H, d, J = 6.0 Hz), 3.25 (3H, s), 4.03 - 4.11 (4H, m), 5.83 (1H, t, J = 6.1 Hz), 6.48 (2H, s), 6.60 (1H, d, J = 7.7 Hz), 7.09 (1H, d, J = 6.1 Hz), 7.18 (1H, t, J = 8.0 Hz), 7.31 (1H, d, J = 8.3 Hz), 7.64 - 7.76 (2H, m)
10963	1.75 - 1.90 (2H, m), 1.91 - 2.01 (2H, m), 2.03 (2H, t, J = 6.9 Hz), 3.24 (2H, d, J = 5.8 Hz), 4.00 (2H, s), 4.09 (2H, t, J = 6.8 Hz), 5.75 (1H, t, J = 6.0 Hz), 6.50 (2H, s), 6.64 (1H, d, J = 7.7 Hz), 7.10 (1H, d, J = 6.1 Hz), 7.16 - 7.25 (2H, m), 7.33 (1H, d, J = 8.3 Hz), 7.73 (1H, d, J = 6.1 Hz), 8.89 - 8.98 (2H, m)
10964	1.09 (3H, t, J = 7.0 Hz), 1.75 - 1.85 (2H, m), 1.91 (2H, dt, J = 8.4, 4.2 Hz), 1.96 (2H, t, J = 6.9 Hz), 2.28 (3H, s), 3.22 (2H, d, J = 5.9 Hz), 3.73 (2H, s), 3.87 (2H, q, J = 7.0 Hz), 4.07 (2H, t, J = 6.8 Hz), 5.62 (1H, d, J = 2.8 Hz), 5.73 (2H, d, J = 2.9 Hz), 6.50 (2H, s), 6.63 (1H, d, J = 7.7 Hz), 7.10 (1H, d, J = 6.1 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.73 (1H, d, J = 6.1 Hz)
10965	1.73 - 1.93 (6H, m), 3.18 (2H, d, J = 5.9 Hz), 3.97 - 4.05 (4H, m), 5.70 (1H, t, J = 6.0 Hz), 6.31 (1H, dd, J = 7.8, 3.2 Hz), 6.49 (2H, s), 6.60 (1H, d, J = 7.7 Hz), 7.03 - 7.09 (1H, m), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.72 (2H, dd, J = 4.6, 1.5 Hz), 8.15 (1H, d, J = 7.8 Hz)
10966	1.77 - 1.87 (4H, m), 1.93 (2H, dt, J = 8.4, 4.2 Hz), 3.19 (2H, d, J = 5.9 Hz), 4.01 (2H, t, J = 6.8 Hz), 4.28 (2H, s), 5.74 (1H, t, J = 5.9 Hz), 6.46 - 6.53 (3H, m), 6.60 (1H, d, J = 7.6 Hz), 7.04 - 7.10 (1H, m), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.72 (1H, d, J = 6.1 Hz), 8.16 (1H, d, J = 6.8 Hz), 8.26 (1H, d, J = 2.7 Hz)

Example No	NMR write-up
10968	1.84 (2H, dd, J = 7.0, 2.5 Hz), 1.95 (2H, dt, J = 8.4, 4.2 Hz), 2.03 (2H, t, J = 6.8 Hz), 3.24 (2H, d, J = 5.8 Hz), 3.88 (2H, s), 4.09 (2H, t, J = 6.8 Hz), 5.83 (1H, t, J = 6.0 Hz), 6.69 (1H, d, J = 7.8 Hz), 6.77 (2H, s), 7.15 (1H, d, J = 6.1 Hz), 7.23 - 7.27 (1H, m), 7.27 - 7.30 (1H, m), 7.32 (1H, ddd, J = 8.5, 2.9, 1.5 Hz), 7.37 (1H, d, J = 8.3 Hz), 7.71 (1H, d, J = 6.3 Hz), 8.13 (1H, dd, J = 4.5, 1.5 Hz), 8.23 (1H, dd, J = 2.8, 0.8 Hz)
10969	1.86 (2H, dd, J = 7.1, 2.4 Hz), 1.98 (2H, d, J = 7.8 Hz), 2.05 (2H, t, J = 6.9 Hz), 3.92 (3H, s), 4.10 (3H, t, J = 6.8 Hz), 5.75 (1H, t, J = 5.9 Hz), 6.30 (1H, s), 6.51 (2H, s), 6.64 (1H, d, J = 7.7 Hz), 6.75 (2H, dd, J = 7.5, 2.5 Hz), 7.11 (1H, d, J = 6.2 Hz), 7.16 - 7.26 (2H, m), 7.33 (1H, d, J = 8.3 Hz), 7.73 (1H, d, J = 6.1 Hz), 7.89 (1H, d, J = 1.0 Hz), 8.38 (1H, s), 8.89 (1H, d, J = 7.6 Hz)
10970	1.84 (2H, dd, J = 7.1, 2.6 Hz), 1.97 (2H, d, J = 8.0 Hz), 2.04 (2H, t, J = 6.9 Hz), 3.08 (2H, d, J = 5.9 Hz), 3.90 (2H, s), 4.09 (2H, t, J = 6.8 Hz), 5.03 (1H, t, J = 6.0 Hz), 6.49 (1H, d, J = 2.2 Hz), 6.58 (1H, dd, J = 7.4, 2.5 Hz), 6.68 (1H, dd, J = 8.7, 2.2 Hz), 6.89 (1H, d, J = 2.5 Hz), 7.13 (1H, d, J = 8.7 Hz), 7.27 (1H, s), 7.36 (1H, d, J = 1.3 Hz), 7.72 (1H, d, J = 1.2 Hz), 8.36 (1H, d, J = 7.3 Hz), 10.86 (1H, s)
10971	1.75 - 1.84 (2H, m), 1.87 - 1.94 (2H, m), 1.98 (2H, t, J = 6.8 Hz), 2.33 (3H, s), 3.21 (2H, d, J = 5.8 Hz), 4.07 (2H, t, J = 6.8 Hz), 4.18 (2H, s), 5.70 (1H, t, J = 5.9 Hz), 6.50 (2H, s), 6.62 (1H, d, J = 7.7 Hz), 6.69 (1H, t, J = 1.0 Hz), 7.06 - 7.12 (1H, m), 7.19 (1H, t, J = 8.0 Hz), 7.32 (1H, d, J = 8.3 Hz), 7.73 (1H, d, J = 6.1 Hz), 8.57 (1H, d, J = 1.1 Hz)
10972	1.75 - 1.83 (2H, m), 1.87 - 2.09 (6H, m), 2.93 (2H, t), 3.22 (2H, d, J = 5.9 Hz), 3.75 (2H, s), 3.82 (2H, t), 4.07 (2H, t, J = 6.8 Hz), 5.55 (1H, d, J = 2.4 Hz), 5.68 - 5.80 (2H, m), 6.50 (2H, s), 6.63 (1H, d, J = 7.7 Hz), 7.10 (1H, d, J = 6.1 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.72 (1H, d, J = 6.1 Hz)
10973	1.84 (2H, dd, J = 7.1, 2.5 Hz), 1.96 (2H, dt, J = 8.3, 4.2 Hz), 2.04 (2H, t, J = 6.8 Hz), 3.24 (2H, d, J = 5.7 Hz), 3.87 (2H, s), 4.10 (2H, t, J = 6.8 Hz), 5.75 (1H, t, J = 6.0 Hz), 6.51 (2H, s), 6.64 (1H, d, J = 7.7 Hz), 6.92 (1H, dd, J = 8.8, 2.4 Hz), 7.10 (1H, d, J = 6.1 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.30 - 7.36 (2H, m), 7.61 (1H, d, J = 8.8 Hz), 7.73 (1H, d, J = 6.1 Hz), 8.57 (1H, s)
10974	1.77 - 1.85 (2H, m), 1.90 - 1.95 (2H, m), 1.99 (2H, t, J = 6.8 Hz), 2.45 (3H, s), 3.22 (2H, d, J = 5.9 Hz), 4.07 (2H, t, J = 6.8 Hz), 4.17 (2H, s), 5.71 (1H, t, J = 5.9 Hz), 6.50 (2H, s), 6.64 (2H, m), 7.09 (1H, d, J = 6.1 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.73 (1H, d, J = 6.1 Hz), 8.34 (1H, d, J = 5.8 Hz)

Example No	NMR write-up
10975	1.78 - 1.87 (2H, m), 1.93 (2H, dt, J = 8.3, 4.2 Hz), 1.99 (2H, t, J = 6.9 Hz), 3.23 (2H, d, J = 5.8 Hz), 3.85 (2H, s), 4.08 (2H, t, J = 6.8 Hz), 5.74 (1H, t, J = 6.0 Hz), 5.84 (1H, d, J = 2.6 Hz), 6.05 (1H, dd, J = 7.9, 2.6 Hz), 6.51 (2H, s), 6.63 (1H, d, J = 7.6 Hz), 7.10 (1H, d, J = 6.1 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.65 (1H, d, J = 7.9 Hz), 7.73 (1H, d, J = 6.1 Hz), 7.76 (1H, t, J = 60.0 Hz)
10976	1.79 - 1.88 (2H, m), 1.88 - 2.10 (4H, m), 3.23 (2H, d, J = 5.8 Hz), 4.08 (2H, t, J = 6.8 Hz), 4.17 (2H, s), 5.69 (1H, t, J = 5.9 Hz), 6.50 (2H, s), 6.64 (1H, d, J = 7.7 Hz), 7.06 - 7.12 (1H, m), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.72 (1H, d, J = 6.1 Hz), 8.13 - 8.20 (2H, m), 8.24 (1H, d, J = 1.3 Hz)
11001	1.77 - 1.84 (2H, m), 1.87 - 1.95 (2H, m), 2.02 (2H, t, J = 6.9 Hz), 3.18 (2H, d, J = 5.8 Hz), 3.30 (3H, s), 3.79 (2H, s), 4.02 (2H, t, J = 6.8 Hz), 5.72 (1H, d, J = 2.8 Hz), 5.85 (1H, dd, J = 7.5, 2.7 Hz), 5.89 (1H, t, J = 6.0 Hz), 6.45 - 6.52 (2H, m), 6.61 (1H, d, J = 7.7 Hz), 7.16 - 7.22 (2H, m), 7.31 (1H, d, J = 8.3 Hz), 7.51 (1H, d, J = 7.5 Hz), 7.72 (1H, d, J = 6.1 Hz)
12001	1.55 (2H, dd, J = 4.5, 1.9 Hz), 1.90 (2H, d, J = 5.6 Hz), 3.30 (3H, s), 3.43 (2H, s), 3.94 (2H, d, J = 6.2 Hz), 4.13 (2H, s), 5.12 (2H, s), 5.76 (1H, d, J = 2.8 Hz), 5.88 (1H, dd, J = 7.5, 2.8 Hz), 5.99 (1H, s), 6.53 (2H, s), 6.69 (1H, d, J = 7.7 Hz), 6.91 (1H, d, J = 6.2 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.25 - 7.50 (6H, m), 7.52 (1H, d, J = 7.6 Hz), 7.70 (1H, d, J = 6.0 Hz)
12007	1.70 (2H, d, J = 4.5 Hz), 1.94 (2H, d, J = 4.9 Hz), 3.25 (2H, s), 3.32 (3H,s), 3.69 (2H, d, J = 4.8 Hz), 4.21 (2H, s), 5.79 (1H, d, J = 2.7 Hz), 5.92 (1H, dd, J = 7.5, 2.8 Hz), 6.26 (1H, t, J = 6.0 Hz), 6.63 (2H, s), 6.72 (1H, d, J = 7.7 Hz), 7.19 (1H, d, J = 6.2 Hz), 7.23 (1H, t, J = 8.0 Hz), 7.39 (1H, d, J = 8.3 Hz), 7.55 (1H, d, J = 7.6 Hz), 7.73 (1H, d, J = 6.2 Hz), 8.35 (2H, s) 2 acid protons and an NH missing
12008	1.69 (2H, d, J = 3.1 Hz), 1.97 (2H, d, J = 4.2 Hz), 3.31 (3H, s), 3.61 (2H,s), 3.98 (2H, d, J = 6.0 Hz), 4.18 (2H, s), 5.79 (1H, d, J = 2.8 Hz), 5.90 (1H, dd, J = 7.5, 2.6 Hz), 6.01 (1H, t, J = 6.2 Hz), 6.54 (2H, s), 6.73 (1H, d, J = 7.8 Hz), 7.00 (1H, d, J = 5.5 Hz), 7.12 - 7.25 (4H, m), 7.35 (1H, d, J = 8.4 Hz), 7.38 - 7.43 (2H, m), 7.53 (1H, d, J = 7.6 Hz), 7.73 (1H, d, J = 6.1 Hz), 8.28 (1H, s) acid proton missing
12009	1.51 - 1.59 (2H, m), 1.84 - 1.95 (2H, m), 2.00 (3H, s), 3.31 (3H, s), 3.49 (2H, s), 3.95 (2H, d, J = 6.2 Hz), 4.14 (2H, s), 5.78 (1H, d, J = 2.7 Hz), 5.89 (1H, dd, J = 7.5, 2.7 Hz), 6.25 (1H, t, J = 6.8 Hz), 6.55 (2H, s), 6.79 (1H, d, J = 7.7 Hz), 6.82 (1H, d, J = 6.2 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.54 (1H, d, J = 7.5 Hz), 7.72 (1H, d, J = 6.1 Hz), 8.30 (1H, s). Formic acid OH not seen

Example No	NMR write-up
12010	1.52 - 1.60 (2H, m), 1.88 - 1.98 (2H, m), 3.31 (3H, s), 3.44 (2H, s), 3.87 (2H, d, J = 5.9 Hz), 4.15 (2H, s), 5.09 (2H, s), 5.78 (1H, d, J = 2.8 Hz), 5.90 (1H, dd, J = 7.5, 2.8 Hz), 6.26 (1H, t, J = 6.1 Hz), 6.48 - 6.59 (1H, m), 6.64 (1H, d, J = 6.0 Hz), 6.91 (1H, d, J = 2.3 Hz), 6.93 (2H, d, J = 2.3 Hz), 7.27 - 7.41 (5H, m), 7.51 (1H, d, J = 6.1 Hz), 7.54 (1H, d, J = 7.5 Hz), 7.90 (1H, d, J = 9.1 Hz), 8.32 (1H, s)
12011	1.34 - 1.47 (2H, m), 1.60 - 1.76 (2H, m), 2.90 (2H, s), 3.31 (3H, s), 4.15 (2H, s), 5.78 (1H, d, J = 2.8 Hz), 5.91 (1H, dd, J = 7.5, 2.7 Hz), 6.15 (1H, t, J = 5.7 Hz), 6.32 (2H, s), 6.52 (1H, d, J = 2.3 Hz), 6.59 (1H, d, J = 5.9 Hz), 6.88 (1H, dd, J = 9.0, 2.4 Hz), 7.53 (1H, d, J = 3.6 Hz), 7.55 (1H, d, J = 1.9 Hz), 7.84 (1H, d, J = 9.0 Hz)
12012	1.49 - 1.63 (2H, m), 1.93 (2H, d, J = 5.5 Hz), 3.04 (3H, s), 3.47 (2H, s), 3.95 (2H, d, J = 6.0 Hz), 4.23 (2H, s), 4.35 (2H, s), 5.12 (2H, s), 5.93 - 6.06 (1H, m), 6.56 (2H, s), 6.71 (1H, d, J = 7.8 Hz), 6.92 (1H, d, J = 6.1 Hz), 7.10 (1H, dd, J = 8.3, 2.5 Hz), 7.14 (1H, d, J = 2.4 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.26 - 7.48 (7H, m), 7.70 (1H, d, J = 6.1 Hz), 8.19 (1H, s). Formic acid OH not seen
12013	1.55 (2H, d, J = 4.4 Hz), 1.90 (2H, d, J = 4.6 Hz), 3.31 (3H, s), 3.38 (2H, s), 3.60 (3H, s), 3.87 (2H, d, J = 6.1 Hz), 4.15 (2H, s), 5.78 (1H, d, J = 2.8 Hz), 5.90 (1H, dd, J = 7.5, 2.7 Hz), 6.25 (1H, t, J = 6.3 Hz), 6.59 (1H, d, J = 2.4 Hz), 6.65 (1H, d, J = 6.1 Hz), 6.93 (3H, dd, J = 9.2, 2.4 Hz), 7.50 (1H, d, J = 6.2 Hz), 7.54 (1H, d, J = 7.5 Hz), 7.89 (1H, d, J = 9.0 Hz), 8.33 (1H, s)
12014	1.65 (2H, dd, J = 4.8, 1.9 Hz), 1.86 - 1.93 (2H, m), 3.04 - 3.11 (2H, m), 3.31 (3H, s), 3.45 - 3.49 (4H, m), 3.81 (2H, d, J = 6.1 Hz), 4.14 (2H, s), 5.78 (1H, d, J = 2.7 Hz), 5.86 - 5.93 (2H, m), 6.53 (2H, d, J = 5.3 Hz), 6.69 (1H, d, J = 7.7 Hz), 6.99 - 7.04 (1H, m), 7.17 - 7.31 (6H, m), 7.37 (1H, d, J = 8.3 Hz), 7.53 (1H, d, J = 7.6 Hz), 7.74 (1H, d, J = 6.1 Hz)
12015	1.63 - 1.72 (2H, m), 1.95 - 2.03 (2H, m), 3.31 (3H, s), 3.66 (2H, s), 3.98 (2H, d, J = 6.3 Hz), 4.20 (2H, s), 5.79 (1H, d, J = 2.8 Hz), 5.90 (1H, dd, J = 7.5, 2.8 Hz), 5.97 (1H, s), 6.52 (2H, s), 6.72 (1H, d, J = 7.7 Hz), 6.98 (1H, s), 7.22 (1H, t, J = 8.0 Hz), 7.29 (1H, ddd, J = 8.7, 6.5, 2.5 Hz), 7.35 (1H, d, J = 8.3 Hz), 7.39 (2H, dd, J = 6.7, 1.8 Hz), 7.53 (1H, d, J = 7.6 Hz), 7.56 - 7.60 (1H, m), 7.72 (1H, d, J = 6.1 Hz)
12016	1.43 (2H, dd, J = 4.5, 1.8 Hz), 1.81 - 1.90 (2H, m), 2.57 (2H, t, J = 7.5 Hz), 2.88 (2H, t, J = 7.5 Hz), 3.30 (3H, s), 3.37 (2H, s), 3.97 (2H, d, J = 6.6 Hz), 4.08 (2H, s), 5.75 (1H, d, J = 2.7 Hz), 5.86 (1H, dd, J = 7.5, 2.7 Hz), 6.21 (1H, t, J = 6.6 Hz), 6.51 (2H, s), 6.80 (2H, dd, J = 15.9, 6.9 Hz), 7.13 - 7.27 (6H, m), 7.33 (1H, d, J = 8.3 Hz), 7.53 (1H, d, J = 7.5 Hz), 7.72 (1H, d, J = 6.0 Hz)

Example No	NMR write-up
12017	1.49 (2H, d, J = 3.9 Hz), 1.82 (2H, d, J = 4.6 Hz), 3.30 (3H, s), 3.36 (2H, s), 3.94 (2H, d, J = 6.4 Hz), 4.15 (2H, s), 4.27 (2H, d, J = 6.0 Hz), 5.78 (1H, d, J = 2.8 Hz), 5.88 (1H, dd, J = 7.5, 2.8 Hz), 6.29 (1H, t, J = 6.7 Hz), 6.48 (2H, s), 6.75 (1H, d, J = 7.8 Hz), 6.85 (1H, d, J = 6.2 Hz), 6.99 (1H, t, J = 6.0 Hz), 7.19 (1H, t, J = 8.0 Hz), 7.22 - 7.27 (1H, m), 7.31 (5H, d, J = 5.6 Hz), 7.52 (1H, d, J = 7.6 Hz), 7.67 (1H, d, J = 6.1 Hz)
12018	1.54 - 1.61 (2H, m), 1.90 - 1.96 (2H, m), 3.01 (3H, s), 3.48 (2H, s), 3.95 (2H, d, J = 6.1 Hz), 4.24 (2H, s), 4.35 (2H, s), 5.12 (2H, s), 6.01 (1H, s), 6.55 (2H, s), 6.71 (1H, d, J = 7.8 Hz), 6.92 (1H, d, J = 6.1 Hz), 6.97 (1H, dd, J = 8.4, 2.3 Hz), 7.10 (1H, d, J = 2.2 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.28 - 7.45 (6H, m), 7.51 (1H, d, J = 8.4 Hz), 7.71 (1H, d, J = 6.0 Hz), 8.25 (1H, s)
12019	1.61 (4H, q, J = 5.9 Hz), 1.72 (2H, p, J = 7.1 Hz), 2.52 (2H, d, J = 5.7 Hz), 2.64 - 2.68 (2H, m), 2.72 (2H, s), 3.31 (3H, s), 3.36 (2H, d, J = 5.2 Hz), 4.09 (2H, s), 5.58 (1H, t, J = 5.3 Hz), 5.76 (1H, d, J = 2.8 Hz), 5.89 (1H, dd, J = 7.5, 2.8 Hz), 6.52 (2H, s), 6.57 (1H, d, J = 7.7 Hz), 6.98 (1H, d, J = 5.9 Hz), 7.09 - 7.14 (1H, m), 7.15 - 7.24 (5H, m), 7.35 (1H, d, J = 8.4 Hz), 7.52 (1H, d, J = 7.6 Hz), 7.73 (1H, d, J = 6.1 Hz)
12020	1.56 (2H, dd, J = 4.6, 1.8 Hz), 1.91 (2H, d, J = 4.7 Hz), 3.30 (3H, s), 3.44 (2H, s), 3.93 (2H, d, J = 6.3 Hz), 4.13 (2H, s), 5.09 (2H, s), 5.76 (1H, d, J = 2.7 Hz), 5.87 (1H, dd, J = 7.5, 2.7 Hz), 5.95 (1H, s), 6.51 (2H, s), 6.69 (1H, d, J = 7.7 Hz), 6.90 (1H, d, J = 6.2 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.27 (1H, s), 7.34 (1H, d, J = 8.3 Hz), 7.40 - 7.55 (3H, m), 7.70 (1H, d, J = 6.1 Hz)
12021	1.59 (2H, dd, J = 4.4, 1.8 Hz), 1.89 - 1.95 (2H, m), 3.31 (3H, s), 3.49 (2H, s), 3.96 (2H, d, J = 6.3 Hz), 4.16 (2H, s), 5.19 (2H, s), 5.78 (1H, d, J = 2.8 Hz), 5.89 (1H, dd, J = 7.5, 2.8 Hz), 5.99 (1H, t, J = 6.5 Hz), 6.51 (2H, s), 6.72 (1H, d, J = 7.8 Hz), 6.94 (1H, d, J = 6.1 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.31 - 7.37 (2H, m), 7.43 (1H, d, J = 7.8 Hz), 7.53 (1H, d, J = 7.6 Hz), 7.71 (1H, d, J = 6.1 Hz), 7.80 - 7.85 (1H, m), 8.56 (1H, ddd, J = 4.8, 1.8, 0.9 Hz)
12022	1.56 (2H, d, J = 2.9 Hz), 1.91 (2H, d, J = 4.1 Hz), 3.30 (3H, s), 3.45 (2H, s), 3.92 (2H, s), 4.13 (2H, s), 5.19 (2H, s), 5.75 (1H, d, J = 2.8 Hz), 5.87 (1H, dd, J = 7.5, 2.8 Hz), 5.96 (1H, t, J = 6.0 Hz), 6.50 (2H, s), 6.67 (1H, s), 6.92 (1H, d, J = 6.0 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.35 - 7.42 (2H, m), 7.45 - 7.57 (3H, m), 7.70 (1H, d, J = 6.1 Hz)

Example No	NMR write-up
12023	1.50 (2H, d, J = 2.8 Hz), 1.85 (2H, d, J = 4.8 Hz), 3.25 (3H, s), 3.39 (2H, s), 3.89 (2H, d, J = 6.2 Hz), 4.08 (2H, s), 5.11 (2H, s), 5.71 (1H, d, J = 2.8 Hz), 5.82 (1H, dd, J = 7.5, 2.8 Hz), 5.93 (1H, t, J = 6.6 Hz), 6.46 (2H, s), 6.65 (1H, d, J = 7.4 Hz), 6.86 (1H, d, J = 6.1 Hz), 7.15 (1H, t, J = 8.0 Hz), 7.29 (1H, d, J = 8.3 Hz), 7.35 (1H, dd, J = 7.5, 5.0 Hz), 7.47 (1H, d, J = 7.6 Hz), 7.66 (1H, d, J = 6.1 Hz), 7.78 (1H, dt, J = 7.9, 2.0 Hz), 8.49 (1H, dd, J = 4.8, 1.7 Hz), 8.59 (1H, d, J = 1.6 Hz)
12024	1.56 (2H, dd, J = 4.6, 1.8 Hz), 1.91 (2H, d, J = 4.6 Hz), 3.30 (3H, s), 3.46 (2H, s), 3.95 (2H, d, J = 6.3 Hz), 4.14 (2H, s), 5.29 (2H, s), 5.76 (1H, d, J = 2.7 Hz), 5.87 (1H, dd, J = 7.6, 2.8 Hz), 5.96 (1H, s), 6.49 (2H, s), 6.69 (1H, s), 6.86 (1H, d, J = 6.1 Hz), 7.17 (1H, t, J = 8.0 Hz), 7.32 (1H, d, J = 8.3 Hz), 7.50 - 7.57 (4H, m), 7.60 (1H, d, J = 6.1 Hz), 7.90 - 7.94 (4H, m)
12025	1.49 - 1.58 (2H, m), 1.79 - 1.89 (2H, m), 3.30 (3H, s), 3.43 (2H, s), 3.92 - 4.00 (2H, m), 4.13 (2H, s), 5.10 (2H, s), 5.76 (1H, d, J = 2.6 Hz), 5.88 (1H, dd, J = 7.6, 2.7 Hz), 6.15 (1H, d, J = 5.5 Hz), 6.44 (1H, s), 6.53 (1H, s), 7.25 - 7.46 (5H, m), 7.52 (1H, d, J = 7.5 Hz), 7.75 (1H, d, J = 5.7 Hz)
12026	1.51 (2H, dd, J = 4.4, 1.8 Hz), 1.88 (2H, d, J = 4.8 Hz), 3.30 (3H, s), 3.35 (2H, s), 3.80 (3H, s), 3.93 (2H, d, J = 6.3 Hz), 4.11 (2H, s), 4.96 (2H, s), 5.72 - 5.77 (1H, m), 5.87 (1H, dd, J = 7.5, 2.7 Hz), 5.99 (1H, s), 6.51 (2H, s), 6.70 (1H, d, J = 7.7 Hz), 6.92 (1H, d, J = 6.1 Hz), 7.20 (1H, t, J = 8.1 Hz), 7.34 (1H, d, J = 8.3 Hz), 7.46 (1H, s), 7.51 (1H, d, J = 7.5 Hz), 7.72 (2H, d, J = 6.3 Hz)
12027	1.43 (9H, s), 1.48 - 1.53 (2H, m), 1.83 - 1.91 (2H, m), 2.54 (2H, s), 3.30 (3H, s), 3.89 (2H, d, J = 5.9 Hz), 4.11 (2H, s), 5.75 (1H, d, J = 2.8 Hz), 5.88 (1H, dd, J = 7.5, 2.8 Hz), 6.59 (2H, s), 6.71 (1H, d, J = 7.7 Hz), 6.97 (1H, d, J = 6.2 Hz), 7.22 (1H, t, J = 8.0 Hz), 7.34 (1H, d, J = 8.3 Hz), 7.52 (1H, d, J = 7.6 Hz), 7.71 (1H, d, J = 6.1 Hz), 8.21 (1H, s)
12028	1.51 (2H, dd, J = 4.5, 1.8 Hz), 1.86 - 1.94 (2H, m), 3.31 (3H, s), 3.58 (2H, s), 3.66 (2H, s), 3.98 (2H, d, J = 6.5 Hz), 4.13 (2H, s), 5.77 (1H, d, J = 2.7 Hz), 5.87 (1H, dd, J = 7.5, 2.7 Hz), 6.15 (1H, t, J = 6.7 Hz), 6.54 (2H, s), 6.79 (2H, dd, J = 7.1, 4.0 Hz), 7.17 - 7.27 (2H, m), 7.24 - 7.35 (5H, m), 7.53 (1H, d, J = 7.5 Hz), 7.69 (1H, d, J = 6.1 Hz)

Example No	NMR write-up
12031	0.96 (2H, q, J = 11.9 Hz), 1.12 (1H, q, J = 10.9 Hz), 1.19 - 1.27 (2H, m), 1.43 - 1.52 (2H, m), 1.64 (3H, t, J = 14.7 Hz), 1.73 (2H, d, J = 12.7 Hz), 1.76 - 1.85 (1H, m), 1.86 - 1.92 (2H, m), 2.14 (2H, d, J = 6.9 Hz), 3.31 (3H, s), 3.48 (2H, s), 3.97 (2H, d, J = 6.6 Hz), 4.13 (2H, s), 5.77 (1H, d, J = 2.7 Hz), 5.89 (1H, dd, J = 7.5, 2.7 Hz), 6.21 (1H, t, J = 6.7 Hz), 6.51 (2H, s), 6.79 (1H, d, J = 6.2 Hz), 6.81 (1H, d, J = 7.9 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.32 (1H, d, J = 8.3 Hz), 7.53 (1H, d, J = 7.6 Hz), 7.70 (1H, d, J = 6.1 Hz)
12034	1.50 (2H, d, J = 4.4 Hz), 1.90 (2H, d, J = 4.7 Hz), 3.30 (3H, s), 3.60 (2H, s), 3.74 (2H, s), 3.99 (2H, d, J = 6.5 Hz), 4.13 (2H, s), 5.77 (1H, d, J = 2.8 Hz), 5.87 (1H, dd, J = 7.5, 2.8 Hz), 6.16 (1H, t, J = 6.7 Hz), 6.53 (2H, s), 6.78 (2H, dd, J = 13.3, 7.0 Hz), 6.90 (1H, dd, J = 2.2, 1.0 Hz), 7.19 (1H, t, J = 7.9 Hz), 7.25 (1H, dd, J = 8.4, 1.8 Hz), 7.32 (1H, d, J = 8.3 Hz), 7.50 - 7.55 (2H, m), 7.57 (1H, d, J = 1.8 Hz), 7.67 (1H, d, J = 6.1 Hz), 7.97 (1H, d, J = 2.2 Hz)
12035	1.64 (2H, dd, J = 4.6, 1.8 Hz), 1.87 - 1.98 (2H, m), 3.28 (3H, s), 3.39 (2H, s), 4.07 (4H, s), 5.71 (1H, d, J = 2.8 Hz), 5.83 (1H, dd, J = 7.5, 2.7 Hz), 6.22 (1H, t, J = 6.4 Hz), 6.51 (2H, s), 6.78 (1H, d, J = 7.7 Hz), 6.96 - 7.03 (1H, m), 7.23 (1H, t, J = 8.0 Hz), 7.35 (1H, d, J = 8.3 Hz), 7.43 - 7.52 (4H, m), 7.62 (2H, dd, J = 7.6, 1.9 Hz), 7.73 (1H, d, J = 6.1 Hz)
12036	1.58 (2H, dd, J = 4.5, 1.8 Hz), 1.80 - 1.90 (2H, m), 3.31 (3H, s), 3.54 (2H, s), 4.01 (2H, d, J = 6.3 Hz), 4.17 (2H, s), 5.79 (1H, d, J = 2.7 Hz), 5.89 (1H, dd, J = 7.5, 2.8 Hz), 6.20 (1H, t, J = 6.5 Hz), 6.50 (2H, s), 6.75 (1H, dd, J = 7.8, 0.9 Hz), 6.91 - 6.97 (1H, m), 6.98 (1H, d, J = 6.2 Hz), 7.23 (3H, td, J = 8.9, 7.6 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.52 (3H, ddd, J = 7.9, 2.3, 1.3 Hz), 7.72 (1H, d, J = 6.1 Hz), 8.51 (1H, s)
12038	1.48 (2H, d, J = 3.0 Hz), 1.81 (2H, d, J = 3.9 Hz), 2.26 (3H, s), 3.30 (3H, s), 3.94 (2H, d, J = 6.3 Hz), 4.12 (2H, s), 4.27 (2H, d, J = 5.9 Hz), 5.69 (1H, d, J = 1.9 Hz), 5.84 (1H, d, J = 2.3 Hz), 6.31 (1H, t, J = 6.5 Hz), 6.52 (2H, s), 6.74 (1H, d, J = 7.8 Hz), 6.86 (1H, d, J = 6.2 Hz), 7.02 (1H, t, J = 6.5 Hz), 7.17 - 7.25 (2H, m), 7.29 - 7.34 (5H, m), 7.67 (1H, d, J = 6.0 Hz), 2 protons hidden under the water peak
12039	1.49 (2H, d, J = 3.2 Hz), 1.89 (2H, d, J = 4.0 Hz), 2.26 (3H, s), 3.30 (3H, s), 3.57 (2H, s), 3.66 (2H, s), 3.98 (2H, d, J = 6.4 Hz), 4.11 (2H, s), 6.58 (1H, d, J = 2.7 Hz), 5.83 (1H, d, J = 2.4 Hz), 6.16 (1H, t, J = 6.6 Hz), 6.54 (2H, s), 6.79 (2H, d, J = 6.3 Hz), 7..18 - 7.34 (7H, m), 7.70 (1H, d, J = 6.1 Hz)

Example No	NMR write-up
12040	1.50 (2H, dd, J = 4.6, 1.8 Hz), 1.85 - 1.93 (2H, m), 3.33 (3H, s), 3.57 (2H, s), 3.87 (2H, s), 3.98 (2H, d, J = 6.6 Hz), 4.11 (2H, s), 5.75 (1H, d, J = 2.8 Hz), 5.85 (1H, dd, J = 7.5, 2.8 Hz), 6.15 (1H, t, J = 6.7 Hz), 6.54 (3H, d, J = 11.7 Hz), 6.73 - 6.83 (2H, m), 6.90 (1H, d, J = 7.1 Hz), 7.01 (1H, dd, J = 8.1, 7.1 Hz), 7.19 (1H, t, J = 8.0 Hz), 7.25 - 7.35 (3H, m), 7.52 (1H, d, J = 7.6 Hz), 7.67 (1H, d, J = 6.1 Hz), 11.11 (1H, s)
12041	1.57 - 1.64 (2H, m), 1.72 - 1.79 (2H, m), 2.82 (3H, s), 3.30 (3H, s), 3.30 (2H, s), 3.85 (2H, d, J = 6.1 Hz), 4.12 (2H, s), 4.50 (2H, s), 5.74 (1H, d, J = 2.8 Hz), 5.87 (1H, dd, J = 7.5, 2.8 Hz), 6.16 (1H, t, J = 6.2 Hz), 6.47 (2H, s), 6.74 (1H, d, J = 7.8 Hz), 7.06 - 7.11 (1H, m), 7.18 (1H, t, J = 8.0 Hz), 7.23 - 7.39 (6H, m), 7.51 (1H, d, J = 7.5 Hz), 7.71 (1H, d, J = 6.1 Hz)
12042	1.41 - 1.48 (2H, m), 1.82 - 1.89 (2H, m), 2.57 (2H, t, J = 7.5 Hz), 2.86 (2H, t, J = 7.5 Hz), 3.30 (3H, s), 3.38 (2H, s), 3.70 (3H, s), 3.97 (2H, d, J = 6.5 Hz), 4.08 (2H, s), 5.75 (1H, d, J = 2.8 Hz), 5.86 (1H, dd, J = 7.5, 2.8 Hz), 6.22 (1H, t, J = 6.7 Hz), 6.51 (2H, s), 6.72 - 6.88 (5H, m), 7.15 (1H, t, J = 8.0 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.53 (1H, d, J = 7.5 Hz), 7.72 (1H, d, J = 6.1 Hz)
12044	1.42 - 1.51 (2H, m), 1.84 - 1.91 (2H, m), 2.61 - 2.69 (2H, m), 2.94 (2H, t, J = 7.4 Hz), 3.31 (3H, s), 3.43 (2H, s), 3.97 (2H, d, J = 6.5 Hz), 4.11 (2H, s), 5.76 (1H, d, J = 2.7 Hz), 5.87 (1H, dd, J = 7.5, 2.8 Hz), 6.17 (1H, t, J = 6.6 Hz), 6.51 (2H, s), 6.77 (2H, t, J = 6.5 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.46 (1H, t, J = 7.7 Hz), 7.53 (1H, d, J = 7.6 Hz), 7.62 - 7.69 (2H, m), 7.71 (1H, d, J = 6.1 Hz), 7.78 (1H, s)
12045	1.41 (9H, s), 1.53 - 1.61 (2H, m), 1.86 - 1.95 (2H, m), 3.31 (5H, s), 3.85 (2H, d, J = 5.7 Hz), 4.15 (2H, s), 5.78 (1H, d, J = 2.7 Hz), 5.90 (1H, dd, J = 7.5, 2.8 Hz), 6.45 (1H, t, J = 5.9 Hz), 6.66 (1H, d, J = 2.2 Hz), 7.16 (1H, dd, J = 8.9, 2.2 Hz), 7.42 (1H, d, J = 5.8 Hz), 7.54 (1H, d, J = 7.6 Hz), 7.74 (1H, d, J = 8.9 Hz), 8.17 (1H, d, J = 5.8 Hz), 8.85 (1H, s)
12046	1.43 (9H, s), 1.51 - 1.54 (2H, m), 1.88 (2H, d, J = 4.6 Hz), 2.25 (3H, s), 3.30 (3H, s), 3.34 (2H, s), 3.96 (2H, d, J = 6.1 Hz), 4.10 (2H, s), 5.66 (1H, d, J = 2.8 Hz), 5.80 - 5.85 (1H, m), 6.42 (1H, s), 6.78 (1H, d, J = 7.8 Hz), 7.27 (1H, d, J = 8.1 Hz), 7.44 (1H, t, J = 7.9 Hz), 7.93 (1H, d, J = 6.1 Hz), 8.41 (1H, d, J = 5.9 Hz), 9.13 (1H, d, J = 0.8 Hz)
12047	1.29 - 1.36 (2H, m), 1.78 - 1.83 (2H, m), 2.70 (2H, t, J = 7.4 Hz), 3.24 (2H, s), 3.30 (3H, s), 3.37 (2H, t, J = 7.3 Hz), 3.96 (2H, d, J = 6.6 Hz), 4.01 (2H, s), 5.71 (1H, d, J = 2.8 Hz), 5.81 (1H, dd, J = 7.5, 2.7 Hz), 6.21 (1H, t, J = 6.8 Hz), 6.52 (2H, s), 6.76 (1H, d, J = 7.8 Hz), 6.82 (1H, d, J = 6.1 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.50 - 7.58 (2H, m), 7.68 - 7.74 (2H, m), 7.96 - 8.02 (2H, m), 8.53 (1H, d, J = 6.0 Hz), 9.31 (1H, d, J = 0.9 Hz)

Example No	NMR write-up
12048	1.39 - 1.46 (2H, m), 1.83 - 1.89 (2H, m), 2.62 (2H, t, J = 7.3 Hz), 2.95 (2H, t, J = 7.5 Hz), 3.30 (3H, s), 3.40 (2H, s), 3.97 (2H, d, J = 6.5 Hz), 4.08 (2H, s), 5.75 (1H, d, J = 2.8 Hz), 5.85 (1H, dd, J = 7.5, 2.7 Hz), 6.20 (1H, t, J = 6.7 Hz), 6.51 (2H, s), 6.78 (1H, d, J = 7.8 Hz), 6.81 (1H, d, J = 6.2 Hz), 6.95 (1H, t, J = 55.9 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.37 - 7.42 (2H, m), 7.46 (1H, d, J = 5.9 Hz), 7.48 (1H, s), 7.53 (1H, d, J = 7.6 Hz), 7.71 (1H, d, J = 6.0 Hz)
12049	1.45 (2H, d, J = 4.3 Hz), 1.87 (2H, d, J = 4.3 Hz), 2.60 (2H, t, J = 7.5 Hz), 2.89 (2H, t, J = 7.5 Hz), 3.30 (3H, s), 3.40 (2H, s), 3.97 (2H, d, J = 6.6 Hz), 4.09 (2H, s), 5.76 (1H, d, J = 2.7 Hz), 5.86 (1H, dd, J = 7.5, 2.8 Hz), 6.19 (1H, t, J = 6.7 Hz), 6.51 (2H, s), 6.79 (2H, t, J = 6.9 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.23 - 7.30 (3H, m), 7.33 (1H, d, J = 8.3 Hz), 7.36 (1H, s), 7.53 (1H, d, J = 7.6 Hz), 7.71 (1H, d, J = 6.0 Hz)
12050	1.44 (2H, d, J = 4.4 Hz), 1.86 (2H, d, J = 4.6 Hz), 2.61 - 2.69 (2H, m), 2.99 (2H, t, J = 7.5 Hz), 3.30 (3H, s), 3.42 (2H, s), 3.96 (2H, d, J = 6.6 Hz), 4.09 (2H, s), 5.75 (1H, d, J = 2.8 Hz), 5.85 (1H, dd, J = 7.5, 2.7 Hz), 6.18 (1H, t, J = 6.6 Hz), 6.51 (2H, s), 6.78 (2H, t, J = 6.9 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.49 (1H, t, J = 7.7 Hz), 7.53 (1H, d, J = 7.6 Hz), 7.55 (1H, d, J = 8.0 Hz), 7.61 (1H, d, J = 7.6 Hz), 7.65 (1H, s), 7.70 (1H, d, J = 6.0 Hz)
12051	1.46 (2H, s), 1.84 (2H, s), 2.55 (2H, t, J = 7.8 Hz), 2.86 (2H, t, J = 7.7 Hz), 3.30 (3H, s), 3.40 (2H, s), 3.98 (2H, d, J = 6.5 Hz), 4.07 (2H, s), 5.74 (1H, d, J = 2.8 Hz), 5.90 (1H, dd, J = 7.5, 2.7 Hz), 6.23 (1H, s), 6.50 (2H, s), 6.78 (1H, d, J = 7.8 Hz), 6.85 (1H, d, J = 6.3 Hz), 7.08 (1H, t, J = 7.3 Hz), 7.12 (1H, d, J = 7.3 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.32 (1H, d, J = 8.3 Hz), 7.52 (1H, d, J = 7.6 Hz), 7.60 - 7.66 (1H, m), 7.70 - 7.74 (2H, m). One exchangeable proton is not observed
12052	1.23 - 1.27 (2H, m), 1.71 - 1.76 (2H, m), 2.62 (2H, t, J = 7.4 Hz), 3.15 (2H, s), 3.23 (3H, s), 3.33 (2H, t, J = 7.3 Hz), 3.89 (2H, d, J = 6.5 Hz), 3.94 (2H, s), 5.64 (1H, d, J = 2.8 Hz), 5.75 (1H, dd, J = 7.5, 2.8 Hz), 6.14 (1H, t, J = 6.7 Hz), 6.44 (2H, d, J = 5.3 Hz), 6.69 (1H, d, J = 7.8 Hz), 6.75 (1H, d, J = 6.2 Hz), 7.14 (1H, t, J = 8.0 Hz), 7.26 (1H, d, J = 8.3 Hz), 7.43 - 7.51 (3H, m), 7.55 (1H, dd, J = 8.5, 7.1 Hz), 7.65 (1H, d, J = 6.1 Hz), 7.82 (1H, d, J = 8.4 Hz), 8.52 (1H, d, J = 8.5 Hz), 8.83 (1H, dd, J = 4.1, 1.6 Hz)
12053	1.45 (2H, d, J = 4.8 Hz), 1.84 - 1.89 (2H, m), 2.61 (2H, q, J = 7.7 Hz), 2.88 (2H, t, J = 7.4 Hz), 3.31 (3H, s), 3.40 (2H, s), 3.97 (2H, d, J = 6.6 Hz), 4.09 (2H, s), 5.76 (1H, d, J = 2.8 Hz), 5.86 (1H, dd, J = 7.5, 2.8 Hz), 6.19 (1H, t, J = 6.6 Hz), 6.50 (2H, d, J = 5.4 Hz), 6.79 (2H, t, J = 7.1 Hz), 7.21 (2H, td, J = 7.9, 4.1 Hz), 7.26 - 7.41 (3H, m), 7.48 - 7.56 (2H, m), 7.72 (1H, d, J = 6.1 Hz)

Example No	NMR write-up
12054	1.46 - 1.51 (2H, m), 1.86 - 1.91 (2H, m), 2.62 (2H, t, J = 7.3 Hz), 3.32 (3H, s), 3.98 (2H, d, J = 6.6 Hz), 4.12 (2H, s), 5.77 (1H, d, J = 2.8 Hz), 5.89 (1H, dd, J = 7.5, 2.8 Hz), 6.19 (1H, d, J = 7.0 Hz), 6.24 (1H, d, J = 9.3 Hz), 6.51-6.52 (2H, m), 6.79 (2H, d, J = 7.5 Hz), 7.18 - 7.25 (2H, m), 7.34 (1H, d, J = 8.3 Hz), 7.42 (1H, dd, J = 9.3, 2.7 Hz), 7.54 (1H, d, J = 7.6 Hz), 7.73 (1H, d, J = 6.1 Hz), 11.38 (1H, s). 2H are under DMSO peak
12055	1.42 - 1.47 (2H, m), 1.81 - 1.87 (2H, m), 2.74 (2H, t, J = 7.4 Hz), 3.12 (2H, t, J = 7.4 Hz), 3.30 (3H, s), 3.44 (2H, s), 3.98 (2H, d, J = 6.6 Hz), 4.08 (2H, s), 5.74 (1H, d, J = 2.8 Hz), 5.81 (1H, dd, J = 7.5, 2.8 Hz), 6.18 (1H, t, J = 6.7 Hz), 6.50 (2H, d, J = 5.4 Hz), 6.77 (2H, t, J = 6.9 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.32 (1H, d, J = 8.3 Hz), 7.43 - 7.50 (1H, m), 7.52 (1H, d, J = 7.5 Hz), 7.55 - 7.63 (2H, m), 7.86 - 7.92 (2H, m), 8.32 (1H, dd, J = 8.3, 1.8 Hz), 8.87 (1H, dd, J = 4.2, 1.8 Hz)
12056	1.44 - 1.49 (2H, m), 1.84 - 1.93 (2H, m), 2.62 (2H, q, J = 7.2 Hz), 2.91 (2H, t, J = 7.5 Hz), 3.31 (3H, s), 3.43 (2H, s), 3.98 (2H, d, J = 6.5 Hz), 4.10 (2H, s), 5.76 (1H, d, J = 2.8 Hz), 5.87 (1H, dd, J = 7.5, 2.8 Hz), 6.20 (1H, t, J = 6.6 Hz), 6.52 (2H, s), 6.80 (2H, dd, J = 14.7, 7.0 Hz), 7.01 (1H, dd, J = 8.0, 2.5 Hz), 7.14 - 7.25 (4H, m), 7.27 - 7.38 (2H, m), 7.54 (1H, d, J = 7.5 Hz), 7.72 (1H, d, J = 6.1 Hz)
12057	1.67 (2H, dd, J = 4.7, 1.8 Hz), 1.97 (2H, d, J = 4.8 Hz), 3.27 (3H, s), 3.66 (2H, s), 4.11 - 4.21 (4H, m), 5.76 (1H, d, J = 2.8 Hz), 5.86 (1H, dd, J = 7.5, 2.8 Hz), 6.47 (3H, s), 6.77 (1H, d, J = 7.7 Hz), 6.97 - 7.00 (1H, m), 7.02 (1H, td, J = 7.7, 1.3 Hz), 7.13 - 7.17 (1H, m), 7.20 (1H, d, J = 7.9 Hz), 7.30 (1H, d, J = 8.4 Hz), 7.32 - 7.35 (1H, m), 7.39 (1H, ddd, J = 7.9, 1.2, 0.6 Hz), 7.49 (1H, d, J = 7.6 Hz), 7.66 (1H, d, J = 6.0 Hz)
12058	1.51 (2H, dd, J = 4.4, 1.8 Hz), 1.79 - 1.86 (2H, m), 3.31 (3H, s), 3.39 (2H, s), 3.94 (2H, d, J = 6.4 Hz), 4.16 (2H, s), 4.32 (2H, d, J = 5.6 Hz), 5.79 (1H, d, J = 2.7 Hz), 5.89 (1H, dd, J = 7.5, 2.7 Hz), 6.26 (1H, t, J = 6.6 Hz), 6.48 (2H, d, J = 5.5 Hz), 6.75 (1H, d, J = 7.8 Hz), 6.84 (1H, d, J = 6.1 Hz), 6.98 (1H, t, J = 5.9 Hz), 7.13 - 7.23 (3H, m), 7.31 (2H, pd, J = 6.3, 3.5 Hz), 7.40 (1H, td, J = 7.8, 1.9 Hz), 7.53 (1H, d, J = 7.6 Hz), 7.67 (1H, d, J = 6.0 Hz)
12059	1.59 - 1.67 (2H, m), 1.85 - 1.93 (2H, m), 3.31 (3H, s), 3.54 (2H, s), 3.71 (3H, s), 3.98 (2H, d, J = 6.1 Hz), 4.18 (2H, s), 5.79 (1H, d, J = 2.7 Hz), 5.91 (1H, dd, J = 7.5, 2.8 Hz), 6.14 (1H, t, J = 6.4 Hz), 6.51 (2H, s), 6.76 (1H, d, J = 7.8 Hz), 6.84 - 6.92 (1H, m), 6.95 - 7.02 (3H, m), 7.22 (1H, t, J = 8.0 Hz), 7.35 (1H, d, J = 8.3 Hz), 7.54 (1H, d, J = 7.6 Hz), 7.57 (1H, s), 7.72 (1H, d, J = 6.1 Hz), 7.81 - 7.87 (1H, m)

Example No	NMR write-up
12060	1.68 (2H, d, J = 3.0 Hz), 2.02 (2H, d, J = 4.3 Hz), 3.31 (3H, s), 3.61 (2H, s), 4.22 (2H, s), 4.26 (2H, d, J = 6.4 Hz), 5.81 (1H, d, J = 2.8 Hz), 5.91 (1H, dd, J = 7.5, 2.8 Hz), 6.31 (1H, t, J = 6.4 Hz), 6.50 (2H, s), 6.81 (1H, d, J = 7.7 Hz), 6.96 (1H, d, J = 6.2 Hz), 7.23 (1H, t, J = 8.0 Hz), 7.30 - 7.38 (2H, m), 7.46 (2H, t, J = 7.7 Hz), 7.54 (1H, d, J = 7.6 Hz), 7.64 - 7.73 (3H, m), 8.75 (2H, s)
12061	1.57 (2H, d, J = 3.0 Hz), 1.85 (2H, d, J = 4.2 Hz), 3.31 (3H, s), 3.50 (2H, s), 3.71 (3H, s), 3.99 (2H, d, J = 6.1 Hz), 4.17 (2H, s), 5.78 (1H, d, J = 2.8 Hz), 5.89 (1H, dd, J = 7.5, 2.8 Hz), 6.23 (1H, t, J = 6.5 Hz), 6.49 (2H, s), 6.75 (1H, d, J = 7.6 Hz), 6.80 - 6.88 (2H, m), 6.97 (1H, d, J = 6.0 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.32 (1H, d, J = 8.3 Hz), 7.37 - 7.45 (2H, m), 7.53 (1H, d, J = 7.6 Hz), 7.71 (1H, d, J = 6.1 Hz), 8.35 (1H, s)
12062	1.48 (2H, d, J = 2.9 Hz), 1.81 (2H, d, J = 3.6 Hz), 3.30 (3H, s), 3.33 (2H, s), 3.74 (3H, s), 3.93 (2H, d, J = 6.3 Hz), 4.14 (2H, s), 4.19 (2H, d, J = 5.7 Hz), 5.77 (1H, d, J = 2.7 Hz), 5.88 (1H, dd, J = 7.5, 2.8 Hz), 6.30 (1H, t, J = 6.6 Hz), 6.49 (2H, s), 6.75 (1H, d, J = 7.7 Hz), 6.84 (1H, d, J = 6.2 Hz), 6.85 - 6.89 (2H, m), 6.92 (1H, t, J = 5.9 Hz), 7.19 (1H, t, J = 8.1 Hz), 7.23 (2H, d, J = 8.7 Hz), 7.30 (1H, d, J = 8.3 Hz), 7.52 (1H, d, J = 7.6 Hz), 7.67 (1H, d, J = 6.1 Hz)
12063	1.41 (9H, s), 1.53 - 1.59 (2H, m), 1.87 - 1.95 (2H, m), 3.30 (3H, s), 3.34 (2H, s), 3.83 (2H, d, J = 5.8 Hz), 4.14 (2H, s), 5.77 (1H, d, J = 2.8 Hz), 5.90 (1H, dd, J = 7.6, 2.8 Hz), 6.16 (1H, t, J = 6.0 Hz), 6.85 (1H, d, J = 2.3 Hz), 7.30 (1H, dd, J = 8.9, 2.3 Hz), 7.50 - 7.56 (2H, m), 7.65 (1H, d, J = 8.9 Hz), 8.12 (1H, d, J = 5.5 Hz), 8.93 - 8.97 (1H, m)
12064	1.82 (2H, dd, J = 4.5, 1.7 Hz), 1.92 (2H, d, J = 4.4 Hz), 3.47 (3H, s), 3.89 (3H, d, J = 5.2 Hz), 4.19 (3H, s), 5.79 (1H, d, J = 2.7 Hz), 5.88 (1H, dd, J = 7.5, 2.8 Hz), 6.56 (1H, s), 6.97 (0.4H, s), 7.05 (1H, d, J = 8.1 Hz), 7.10 (0.4H, s), 7.23 (0.4H, s), 7.47 (2H, d, J = 7.3 Hz), 7.50 - 7.57 (2H, m), 7.62 (2H, dd, J = 7.5, 3.6 Hz), 7.70 (1H, d, J = 8.3 Hz), 8.10 (1H, dd, J = 4.9, 1.2 Hz), 8.29 (1H, d, J = 2.8 Hz), 8.80 (2H, s), 13.10 (0.8H, s)
12065	1.77 (2H, dd, J = 4.4, 1.8 Hz), 1.95 - 2.00 (2H, m), 3.31 (3H, s), 3.43 (2H, s), 3.97 (2H, d, J = 5.5 Hz), 4.20 (2H, s), 5.79 (1H, d, J = 2.7 Hz), 5.89 (1H, dd, J = 7.5, 2.8 Hz), 5.95 (1H, t, J = 5.6 Hz), 6.53 (2H, s), 6.70 (3H, dd, J = 6.7, 1.6 Hz), 7.08 - 7.14 (1H, m), 7.24 (1H, t, J = 8.0 Hz), 7.39 (1H, d, J = 8.3 Hz), 7.53 (1H, d, J = 7.6 Hz), 7.72 (1H, d, J = 6.1 Hz), 8.03 - 8.09 (2H, m)

Example No	NMR write-up
12067	1.48 - 1.54 (2H, m), 1.80 - 1.85 (2H, m), 3.31 (3H, s), 3.40 (2H, s), 3.81 (3H, s), 3.93 (2H, d, J = 6.3 Hz), 4.16 (2H, s), 4.25 (2H, d, J = 5.8 Hz), 5.78 (1H, d, J = 2.7 Hz), 5.89 (1H, dd, J = 7.5, 2.7 Hz), 6.27 (1H, t, J = 6.5 Hz), 6.48 (2H, s), 6.74 (1H, d, J = 7.7 Hz), 6.78 (1H, t, J = 6.0 Hz), 6.84 (1H, d, J = 6.1 Hz), 6.92 (1H, td, J = 7.4, 1.1 Hz), 6.95 - 6.99 (1H, m), 7.16 - 7.26 (3H, m), 7.30 (1H, d, J = 8.3 Hz), 7.53 (1H, d, J = 7.6 Hz), 7.66 (1H, d, J = 6.1 Hz)
12068	1.55 - 1.61 (2H, m), 1.84 - 1.90 (2H, m), 3.31 (3H, s), 3.55 (2H, s), 3.98 (2H, d, J = 6.2 Hz), 4.18 (2H, s), 5.79 (1H, d, J = 2.8 Hz), 5.90 (1H, dd, J = 7.6, 2.8 Hz), 6.18 (1H, t, J = 6.4 Hz), 6.51 (2H, s), 6.75 (1H, d, J = 7.8 Hz), 6.96 (1H, d, J = 6.2 Hz), 7.10 - 7.16 (2H, m), 7.17 - 7.24 (2H, m), 7.33 (1H, d, J = 8.3 Hz), 7.53 (1H, d, J = 7.6 Hz), 7.55 - 7.61 (1H, m), 7.71 (1H, d, J = 6.1 Hz), 8.25 (1H, s)
12069	1.49 (2H, dd, J = 4.5, 1.8 Hz), 1.80 - 1.85 (2H, m), 3.30 (3H, s), 3.38 (2H, s), 3.93 (2H, d, J = 6.4 Hz), 4.15 (2H, s), 4.35 (2H, d, J = 5.9 Hz), 5.78 (1H, d, J = 2.8 Hz), 5.88 (1H, dd, J = 7.5, 2.7 Hz), 6.25 (1H, t, J = 6.5 Hz), 6.48 (2H, s), 6.74 (1H, d, J = 7.7 Hz), 6.81 (1H, d, J = 6.1 Hz), 7.11 (1H, t, J = 6.0 Hz), 7.18 (1H, t, J = 8.0 Hz), 7.30 (1H, d, J = 8.3 Hz), 7.53 (1H, d, J = 7.6 Hz), 7.54 - 7.66 (5H, m)
12070	1.47 - 1.51 (2H, m), 1.79 - 1.85 (2H, m), 3.30 (3H, s), 3.36 (2H, s), 3.94 (2H, d, J = 6.3 Hz), 4.14 (2H, s), 4.35 (2H, d, J = 5.9 Hz), 5.77 (1H, d, J = 2.7 Hz), 5.88 (1H, dd, J = 7.5, 2.8 Hz), 6.31 (1H, t, J = 6.6 Hz), 6.50 (2H, s), 6.75 (1H, d, J = 7.7 Hz), 6.83 (1H, d, J = 6.1 Hz), 6.93 (1H, dd, J = 2.2, 1.0 Hz), 7.02 (1H, t, J = 6.0 Hz), 7.19 (1H, t, J = 8.0 Hz), 7.26 - 7.33 (2H, m), 7.52 (2H, d, J = 7.8 Hz), 7.57 (1H, d, J = 1.7 Hz), 7.60 (1H, s), 7.97 (1H, d, J = 2.2 Hz)
12071	1.62 (2H, dd, J = 4.8, 1.8 Hz), 1.90 (2H, d, J = 4.7 Hz), 3.28 (4H, d, J = 2.4 Hz), 3.44 (2H, s), 3.81 (3H, s), 4.09 (3H, d, J = 5.8 Hz), 5.71 (1H, d, J = 2.8 Hz), 5.84 (1H, dd, J = 7.6, 2.8 Hz), 6.22 (1H, t, J = 6.5 Hz), 6.50 (2H, d, J = 4.3 Hz), 6.76 (1H, d, J = 7.8 Hz), 6.96 - 7.03 (3H, m), 7.23 (1H, t, J = 8.0 Hz), 7.34 (1H, d, J = 8.3 Hz), 7.49 (1H, d, J = 7.6 Hz), 7.60 - 7.66 (2H, m), 7.73 (1H, d, J = 6.1 Hz)
12072	1.32 (2H, dd, J = 4.4, 1.8 Hz), 1.57 - 1.70 (2H, m), 3.92 (2H, d, J = 5.9 Hz), 4.08 (2H, s), 4.32 (2H, d, J = 5.8 Hz), 5.73 (1H, d, J = 2.7 Hz), 5.87 (1H, dd, J = 7.5, 2.7 Hz), 5.93 (1H, s), 6.75 (2H, s), 6.87 (1H, d, J = 6.2 Hz), 6.96 (1H, t, J = 5.9 Hz), 7.20 (1H, dd, J = 12.7, 9.1 Hz), 7.24 - 7.29 (1H, m), 7.35 (4H, d, J = 4.4 Hz), 7.52 (1H, d, J = 7.6 Hz), 7.57 - 7.62 (2H, m), 8.22 (2H, s)

Example No	NMR write-up
13001	1.61 (2H, d, J = 3.1 Hz), 1.92 (2H, d, J = 3.1 Hz), 3.31 (3H, s), 3.45 (2H,s), 3.52 (2H, d, J = 5.8 Hz), 4.47 (2H, s), 5.01 (2H, s), 5.67 (1H, s), 5.87 (1H, dd, J = 7.5, 2.5 Hz), 6.00 (1H, t, J = 6.0 Hz), 6.49 (2H, s), 6.68 (1H, d, J = 7.7 Hz), 7.16 (1H, d, J = 6.2 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.27 - 7.35 (6H, m), 7.51 (1H, d, J = 7.6 Hz), 7.71 (1H, d, J = 6.1 Hz), 8.26 (1H, s) acid proton missing
13002	1.59 - 1.72 (1H, m), 1.97 - 2.19 (3H, m), 3.83 - 4.21 (4H, m), 4.59 - 4.91 (2H, m), 4.93 - 5.14 (2H, m), 5.92 - 6.11 (1H, m), 6.52 (2H, s), 6.69 (1H, dd, J = 7.8, 4.2 Hz), 7.10 - 7.45 (7H, m), 7.71 (1H, d, J = 6.1 Hz), 8.28 (1H, s). 5 protons hidden beneath water peak. Rotamers present
13003	1.60 (2H, s), 1.92 (5H, s), 3.32 (3H, s), 3.49 - 3.58 (4H, m), 4.60 (2H, s), 5.66 (1H, s), 5.85 - 5.92 (1H, m), 5.98 (1H, s), 6.50 (2H, s), 6.68 (1H, d, J = 7.8 Hz), 7.17 (1H, d, J = 6.1 Hz), 7.21 (1H, t, J = 8.0 Hz), 7.34 (1H, d, J = 8.2 Hz), 7.53 (1H, d, J = 7.6 Hz), 7.73 (1H, d, J = 6.1 Hz), 8.21 (1H, s)
13004	1.74 (2H, s), 2.01 (2H, s), 3.28 (3H, s), 3.59 (2H, d, J = 5.9 Hz), 3.67 (2H, s), 4.51 (2H, s), 5.68 (1H, d, J = 2.8 Hz), 5.89 (1H, dd, J = 7.5, 2.8 Hz), 6.06 (1H, d, J = 6.3 Hz), 6.49 (2H, s), 6.73 (1H, d, J = 7.7 Hz), 7.15 - 7.38 (6H, m), 7.51 (2H, dd, J = 7.4, 5.1 Hz), 7.73 (1H, d, J = 5.9 Hz)
13005	1.34 (9H, s), 1.57 (2H, s), 1.90 (2H, d, J = 8.1 Hz), 3.26 - 3.31 (2H, m), 3.34 (3H, s), 3.48 - 3.53 (2H, m), 4.41 (2H, s), 5.69 (1H, d, J = 2.8 Hz), 5.90 (1H, dd, J = 7.5, 2.7 Hz), 5.98 (1H, t), 6.47 (2H, s), 6.67 (1H, d, J = 7.8 Hz), 7.17 (1H, d, J = 6.4 Hz), 7.20 (1H, d, J = 7.9 Hz), 7.32 (1H, d, J = 8.4 Hz), 7.53 (1H, d, J = 7.6 Hz), 7.72 (1H, d, J = 6.1 Hz)
13006	1.68 (2H, s), 1.92 (2H, s), 3.22 (3H, s), 3.50 (2H, d, J = 6.0 Hz), 3.56 (2H, bs) 4.45 (2H, s), 5.62 (1H, d, J = 2.7 Hz), 5.84 (1H, dd, J = 7.6, 2.8 Hz), 5.98 (1H, s), 6.41 (2H, s), 6.65 (1H, d, J = 7.6 Hz), 7.03 (1H, s), 7.09 - 7.18 (3H, m), 7.27 (3H, t, J = 9.5 Hz), 7.44 (1H, d, J = 7.6 Hz), 7.66 (1H, d, J = 6.1 Hz), 8.48 (1H, s)
13007	1.54 (2H, dd, J = 4.8, 1.9 Hz), 1.82 (2H, d, J = 4.8 Hz), 3.08 (2H, s), 3.32 (3H, s), 3.53 (2H, d, J = 5.8 Hz), 4.20 (2H, s), 5.80 (1H, d, J = 2.8 Hz), 5.90 (1H, dd, J = 7.5, 2.7 Hz), 6.01 (1H, t, J = 6.0 Hz), 6.51 (2H, s), 6.65 - 6.71 (1H, m), 7.12 - 7.17 (1H, m), 7.20 (1H, t, J = 8.0 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.55 (1H, d, J = 7.6 Hz), 7.72 (1H, d, J = 6.1 Hz), 8.27 (1H, s)
13008	1.46 - 1.55 (2H, m), 1.82 - 1.92 (2H, m), 2.48 (2H, t, J = 8.3 Hz), 2.79 (2H, t, J = 7.7 Hz), 3.31 (3H, s), 3.42 (2H, s), 3.47 (2H, d, J = 5.9 Hz), 4.61 (2H, s), 5.67 (1H, d, J = 2.7 Hz), 5.88 (1H, dd, J = 7.5, 2.8 Hz), 5.93 (1H, t, J = 6.0 Hz), 6.48 (2H, s), 6.63 (1H, d, J = 7.8 Hz), 7.11 - 7.28 (7H, m), 7.33 (1H, d, J = 8.3 Hz), 7.53 (1H, d, J = 7.6 Hz), 7.72 (1H, d, J = 6.1 Hz)

Example No	NMR write-up
13009	1.53 - 1.61 (2H, m), 1.83 - 1.90 (2H, m), 3.26 (3H, s), 3.40 (2H, s), 3.47 (2H, d, J = 5.8 Hz), 4.42 (2H, s), 5.00 (2H, s), 5.60 (1H, s), 5.80 (1H, d, J = 7.5 Hz), 5.94 (1H, t, J = 6.0 Hz), 6.43 (2H, s), 6.63 (1H, d, J = 7.6 Hz), 7.11 (1H, dd, J = 6.4, 0.8 Hz), 7.15 (1H, t, J = 8.0 Hz), 7.24 - 7.34 (2H, m), 7.45 (1H, d, J = 7.6 Hz), 7.64 - 7.72 (2H, m), 8.45 (1H, d, J = 4.8 Hz), 8.49 (1H, s)
13010	1.49 - 1.55 (2H, m), 1.87 - 1.92 (2H, m), 2.54 (2H, t, J = 7.6 Hz), 2.81 (2H, t, J = 7.5 Hz), 3.32 (3H, s), 3.45 (2H, s), 3.48 (2H, d, J = 5.9 Hz), 4.61 (2H, s), 5.67 (1H, d, J = 2.7 Hz), 5.88 (1H, dd, J = 7.5, 2.8 Hz), 5.94 (1H, t, J = 5.9 Hz), 6.48 (2H, s), 6.64 (1H, d, J = 7.8 Hz), 7.14 (1H, d, J = 6.2 Hz), 7.20 (1H, t, J = 8.0 Hz), 7.26 (1H, dd, J = 7.8, 4.8 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.53 (1H, d, J = 7.5 Hz), 7.64 (1H, d, J = 7.8 Hz), 7.72 (1H, d, J = 6.1 Hz), 8.37 (1H, dd, J = 4.8, 1.7 Hz), 8.45 (1H, d, J = 2.3 Hz)
13011	1.61 - 1.66 (2H, m), 1.78 - 1.84 (2H, m), 2.76 (3H, s), 3.32 (3H, s), 3.35 (2H, s), 3.49 (2H, d, J = 5.8 Hz), 4.44 (2H, s), 4.50 (2H, s), 5.73 (1H, d, J = 2.7 Hz), 5.90 (1H, dd, J = 7.5, 2.8 Hz), 5.94 (1H, t, J = 6.0 Hz), 6.47 (2H, s), 6.66 (1H, d, J = 7.8 Hz), 7.15 - 7.34 (8H, m), 7.54 (1H, d, J = 7.5 Hz), 7.72 (1H, d, J = 6.1 Hz)
13012	1.55 (2H, dd, J = 4.4, 1.8 Hz), 1.85 (2H, d, J = 4.5 Hz), 3.31 (3H, s), 3.40 (2H, s), 3.52 (2H, d, J = 5.8 Hz), 4.20 (2H, d, J = 5.9 Hz), 4.58 (2H, s), 5.66 (1H, d, J = 2.7 Hz), 5.88 (1H, dd, J = 7.5, 2.8 Hz), 5.95 (1H, t, J = 5.9 Hz), 6.47 (2H, s), 6.67 (1H, d, J = 7.8 Hz), 6.96 (1H, t, J = 6.0 Hz), 7.16 - 7.36 (8H, m), 7.52 (1H, d, J = 7.5 Hz), 7.72 (1H, d, J = 6.1 Hz)
13013	1.65 (2H, dd, J = 4.6, 1.8 Hz), 1.91 - 2.05 (2H, m), 3.32 (3H, s), 3.51 (2H, s), 3.55 (2H, d, J = 6.0 Hz), 4.50 (2H, s), 5.08 (2H, s), 5.69 (1H, d, J = 2.8 Hz), 5.88 (1H, dd, J = 7.5, 2.8 Hz), 6.01 (1H, t, J = 6.1 Hz), 6.48 (2H, s), 6.70 (1H, d, J = 7.7 Hz), 7.15 - 7.25 (2H, m), 7.28 - 7.41 (3H, m), 7.51 (1H, d, J = 7.5 Hz), 7.70 - 7.79 (2H, m), 8.52 (1H, ddd, J = 4.8, 1.8, 0.9 Hz)
13014	1.72 (2H, dd, J = 4.7, 1.9 Hz), 1.88 - 1.95 (2H, m), 2.97 - 3.04 (2H, m), 3.32 (3H, s), 3.40 - 3.47 (2H, m), 3.48 - 3.54 (4H, m), 4.35 (2H, s), 5.75 (1H, d, J = 2.8 Hz), 5.78 (1H, dd, J = 7.5, 2.7 Hz), 6.01 (1H, t, J = 6.0 Hz), 6.49 (2H, s), 6.69 (1H, d, J = 7.7 Hz), 7.15 - 7.36 (8H, m), 7.55 (1H, d, J = 7.5 Hz), 7.73 (1H, d, J = 6.1 Hz)
13015	1.62 (4H, s), 1.67 - 1.73 (2H, m), 2.53 (2H, s), 2.60 - 2.64 (2H, m), 2.77 (2H, s), 3.32 (3H, s), 3.44 (2H, d, J = 5.6 Hz), 4.06 (2H, s), 5.78 (1H, d, J = 2.7 Hz), 5.85 - 5.94 (2H, m), 6.48 (2H, s), 6.64 (1H, d, J = 7.8 Hz), 7.11 - 7.26 (7H, m), 7.31 (1H, d, J = 8.3 Hz), 7.53 (1H, d, J = 7.6 Hz), 7.71 (1H, d, J = 6.1 Hz)

Example No	NMR write-up
13016	1.49 - 1.58 (2H, m), 1.85 - 1.95 (2H, m), 2.60 - 2.66 (2H, m), 2.95 (2H, t, J = 7.5 Hz), 3.27 - 3.31 (2H, m), 3.47 - 3.56 (5H, m), 4.59 (2H, s), 5.65 (1H, d, J = 2.7 Hz), 5.87 (1H, dd, J = 7.5, 2.7 Hz), 5.96 (1H, t, J = 6.0 Hz), 6.48 (2H, s), 6.66 (1H, d, J = 7.7 Hz), 7.13 (1H, ddd, J = 7.6, 4.9, 1.2 Hz), 7.14 - 7.17 (1H, m), 7.20 (1H, t, J = 8.0 Hz), 7.25 (1H, d, J = 7.8 Hz), 7.33 (1H, d, J = 8.3 Hz), 7.52 (1H, d, J = 7.6 Hz), 7.65 (1H, t), 7.73 (1H, d, J = 6.1 Hz), 8.39 (1H, ddd, J = 4.9, 1.9, 1.0 Hz)
13017	1.49 - 1.54 (2H, m), 1.89 (2H, d, J = 4.5 Hz), 2.90 (2H, t, J = 7.8 Hz), 3.32 (3H, s), 3.45 (2H, s), 3.48 (2H, d, J = 5.8 Hz), 4.61 (2H, s), 5.67 (1H, d, J = 2.8 Hz), 5.88 (1H, dd, J = 7.6, 2.7 Hz), 5.94 (1H, t, J = 6.0 Hz), 6.47 (2H, d, J = 5.5 Hz), 6.64 (1H, d, J = 7.7 Hz), 7.12 - 7.21 (3H, m), 7.25 (1H, t, J = 7.4 Hz), 7.33 (3H, ddd, J = 8.1, 4.5, 3.1 Hz), 7.53 (1H, d, J = 7.6 Hz), 7.72 (1H, d, J = 6.1 Hz). 2H under DMSO peak.
13018	1.74 (2H, dd, J = 4.6, 1.8 Hz), 1.97 (2H, d, J = 5.5 Hz), 3.28 (3H, s), 3.54 (2H, d, J = 5.9 Hz), 3.68 (2H, s), 4.76 (2H, s), 5.80 (1H, d, J = 2.7 Hz), 5.86 (1H, dd, J = 7.5, 2.7 Hz), 5.99 (1H, t, J = 6.0 Hz), 6.43 (2H, s), 6.67 (1H, d, J = 7.7 Hz), 6.97 (1H, td, J = 7.7, 1.3 Hz), 7.08 (1H, td, J = 7.7, 1.2 Hz), 7.12 - 7.20 (2H, m), 7.23 - 7.33 (3H, m), 7.49 (1H, d, J = 7.5 Hz), 7.68 (1H, d, J = 6.1 Hz)
13019	1.61 - 1.68 (2H, m), 1.86 - 1.92 (2H, m), 3.31 (3H, s), 3.53 (2H, d, J = 5.6 Hz), 3.57 (2H, s), 4.63 (2H, s), 5.71 (1H, d, J = 2.7 Hz), 5.89 (1H, dd, J = 7.5, 2.8 Hz), 5.96 (1H, t, J = 5.8 Hz), 6.48 (2H, s), 6.68 (1H, d, J = 7.7 Hz), 6.91 (1H, t, J = 7.3 Hz), 7.17 - 7.24 (4H, m), 7.34 (1H, d, J = 8.3 Hz), 7.47 (2H, dd, J = 8.6, 1.3 Hz), 7.53 (1H, d, J = 7.5 Hz), 7.72 (1H, d, J = 6.1 Hz), 8.56 (1H, s)
13020	1.62 (2H, dd, J = 4.6, 1.7 Hz), 1.90 - 1.95 (2H, m), 3.47 (3H, s), 3.53 (2H, d, J = 5.8 Hz), 4.45 (2H, s), 5.08 (2H, s), 5.62 (1H, s), 5.84 (1H, d, J = 7.6 Hz), 5.99 (1H, t, J = 6.0 Hz), 6.47 (2H, s), 6.68 (1H, d, J = 7.7 Hz), 7.13 - 7.24 (2H, m), 7.28 - 7.36 (3H, m), 7.43 (2H, d, J = 7.2 Hz), 7.49 (1H, d, J = 7.5 Hz), 7.72 (1H, d, J = 6.1 Hz)
13021	1.59 (d, J = 3.6 Hz, 2H), 1.90 – 1.97 (m, 2H), 3.30 (s, 3H), 3.53 (d, J = 5.8 Hz, 2H), 3.58 (s, 2H), 3.63 (s, 2H), 4.59 (s, 2H), 5.64 (d, J = 2.8 Hz, 1H), 5.86 (dd, J = 7.5, 2.7 Hz, 1H), 5.98 (t, J = 6.0 Hz, 1H), 6.48 (d, J = 4.4 Hz, 2H), 6.68 (d, J = 7.7 Hz, 1H), 7.14 – 7.17 (m, 1H), 7.18 – 7.25 (m, 4H), 7.25 – 7.30 (m, 2H), 7.34 (d, J = 8.3 Hz, 1H), 7.51 (d, J = 7.6 Hz, 1H), 7.73 (d, J = 6.1 Hz, 1H)

Example No	NMR write-up
13022	1.57 (2H, dd, J = 4.5, 1.8 Hz), 1.82 - 1.95 (2H, m), 3.32 (3H, s), 3.37 (2H, s), 3.50 (2H, d, J = 5.8 Hz), 3.78 (3H, s), 4.46 (2H, s), 4.84 (2H, s), 5.66 (1H, s), 5.81 - 5.90 (1H, m), 5.98 (1H, t, J = 6.1 Hz), 6.46 (2H, d, J = 5.5 Hz), 6.66 (1H, d, J = 7.7 Hz), 7.15 (1H, d, J = 6.1 Hz), 7.19 (1H, t, J = 8.0 Hz), 7.32 (1H, d, J = 8.3 Hz), 7.36 (1H, s), 7.52 (1H, d, J = 7.6 Hz), 7.64 (1H, s), 7.71 (1H, d, J = 6.1 Hz)

Biological Methods

Determination of FXIIa inhibition

In vitro inhibition of Factor XIIa was determined using an IC_{50} assay based on standard literature methods (see e.g Baeriswyl et al., ACS Chem. Biol., 2015, 10 (8) 1861; Bouckaert et al., European Journal of Medicinal Chemistry 110 (2016) 181). Human Factor XIIa (Enzyme Research Laboratories) was incubated at 25 °C with the fluorogenic substrate H-DPro-Phe-Arg-AFC (Peptide Protein Science) and various concentrations of the test compound. Protease activity was measured by monitoring the accumulation of liberated fluorescence from the substrate over 5 min at 25 °C. The linear rate of fluorescence increase per minute was expressed as percentage (%) activity. The Km for the cleavage of the substrate by FXIIa was determined by standard transformation of the Michaelis-Menten equation. The compound inhibitor assays were performed at substrate Km concentration. IC_{50} values were calculated as the concentration of inhibitor giving 50% inhibition (IC_{50}) of the uninhibited enzyme activity (100%). Data acquired from this assay are shown in Table 16 below using the following scale:

Category	IC_{50} (nM)
AA	1 - 10
A	10 - 100
B	100 - 300
C	300 – 1,000
D	1,000 – 3,000
E	3,000 – 10,000
F	10,000 – 40,000
G	40,000 - 100,000

For the test compounds that did not achieve 50% inhibition the following scale is used:

Category	
H1	>20% inhibition @ 40 µM
H2	>20% inhibition @ 100 µM
H3	>20% inhibition @ 400 µM

Table 16: Human FXIIa data, molecular weight and LCMS data

Example No	Human FXIIa IC50 (nM)	Molecular weight	LCMS Mass Ion
1001	B	385.5	386.2
1002	B	389.5	390.2
1002.1	B	389.5	390.2
1002.2	C	389.5	390.2
1004	E	374.5	375.2
1005.1	C	391.6	392.2
1006	B	399.5	400.2
1009	F	359.4	360.3
1010	C	393.9	394.3
1011	F	370.5	371.3
1012	D	373.5	374.3
1013	C	386.5	387.2
1014	D	384.5	385.2
1015	F	389.5	390.2
1016	E	388.5	389.2
1017	B	385.5	386.2
1018	C	385.5	386.2
1019	C	376.5	377.2
1101	E	385.5	386.2
1105	E	385.5	386.2
1109	C	400.5	401.2
1110	E	386.5	387.1
1113	D	400.5	401.2

Example No	Human FXIIa IC50 (nM)	Molecular weight	LCMS Mass Ion
1118	D	375.5	376.2
1125	F	385.5	386.2
1126	F	371.5	372.2
1127	E	386.5	386.2
1129	H2	393.9	394.2/396.2
1130	C	397.9	398.2
1131	F	371.4	372.1
1132	F	449.5	450.1
1133	B	401.3	400.5
1134	B	391.3	390.5
1135	C	387.3	386.5
2020	A	401.5	402.2
2022	B	401.5	402.2
2204	C	453.4	454.4
2205	C	392.5	393.2
2206	D	470.5	471.2
2207	D	402.5	403.1
2208	E	388.4	389.2
2210	D	402.5	403.2
2211	B	430.5	431.2
2212	A	415.5	416.4
4401	C	373.5	374.2
5003	B	373.5	374.3
6601	A	401.5	402.2
6602	A	401.5	402.2
6605	E	389.5	390.3
6606	D	409.9	410.1
6608	C	453.4	454.3
6609	B	392.5	393.2
6610	C	405.5	406.2
6611	D	409.9	410.1

Example No	Human FXIIa IC50 (nM)	Molecular weight	LCMS Mass Ion
6612	D	402.5	403.2
6613	C	451.5	452.1
6614	B	402.5	403.2
6615	E	470.5	471.4
6616	C	402.5	403.4
6617	A	415.5	416.4
6618	A	416.5	417.4
6619	C	401.5	402.3
6620	C	452.5	453.4
6621	B	430.5	431.4
6622	A	415.5	416.4
6623	E	402.5	403.4
6624	A	415.5	416.4
6625	C	419.5	420.4
6626	A	415.5	416.3
6627	D	469.5	470.3
6628	B	430.5	431.4
6629	A	402.5	403.4
6630	B	469.5	470.4
6631	B	431.5	432.4
6633	B	415.5	416.4
6634	D	402.5	403.4
6635	F	430.5	431.5
6636	E	430.5	431.4
6637	B	430.5	431.4
6638	D	403.4	404.3
6639	A	441.5	442.3
6640	B	444.5	445.3
6641	B	443.5	444.4
6642	B	416.5	417.4
6643	C	442.5	443.3

Example No	Human FXIIa IC50 (nM)	Molecular weight	LCMS Mass Ion
6644	C	451.5	452.2
6645	F	335.4	336.2
6646	G	335.4	336.2
6647	G	336.4	337.2
6648	F	336.4	337.3
6649	F	352.4	353.3
6650	B	444.5	445.3
6651	H1	424.9	425.1
6653	C	444.5	445.3
6654	F	444.5	445.3
6656	H2	416.5	417.5
6658	F	374.4	375.3
6659	G	431.5	432.4
6660	E	365.4	366.1
6661	F	350.4	351.3
6663	H2	380.4	381.4
7702	C	430.5	431.2
7703	B	429.5	430.2
7704	C	430.5	431.2
8801	F	385.5	386.4
8803	D	399.5	400.3
8804	D	399.5	400.6
8805	D	399.5	400.4
8806	B	399.5	400.2
8807	C	399.5	400.2
8808	F	385.5	386.2
9001	F	385.5	386.1
9002	F	385.5	386.6
9003	F	385.5	386.6
10901	A	415.5	416.2
10903	C	419.5	420.4

Example No	Human FXIIa IC50 (nM)	Molecular weight	LCMS Mass Ion
10904	A	415.5	416.2
10906	B	406.5	407.2
10907	D	403.5	404.2
10908	C	419.5	420.2
10909	D	423.9	424.1
10910	B	467.5	468.2
10911	E	406.5	407.2
10912	F	377.4	378.2
10914	E	376.5	377.2
10915	F	376.5	377.2
10918	H3	383.9	384.3
10919	H3	383.9	384.3
10920	B	429.5	430.4
10921	G	434.9	435.3
10922	C	449.9	450.6
10923	B	429.5	430.4
10924	B	449.9	450.3
10925	A	429.5	430.4
10926	A	416.5	417.2
10928	A	420.5	421.2
10929	C	416.5	417.4
10930	A	429.5	430.4
10931	A	430.5	431.4
10932	B	483.5	484.4
10933	D	440.9	441.0
10934	C	434.5	435.4
10936	E	366.4	367.3
10937	E	377.4	378.4
10938	C	444.5	445.4
10939	C	458.6	459.4
10940	B	407.5	408.3

Example No	Human FXIIa IC50 (nM)	Molecular weight	LCMS Mass Ion
10941	C	430.5	431.4
10942	B	413.5	414.3
10943	D	406.5	407.4
10944	D	406.5	407.4
10945	E	406.5	407.4
10946	E	380.4	381.4
10948	D	419.5	420.4
10949	C	448.6	449.4
10951	C	474.5	475.3
10952	C	392.5	393.2
10953	B	390.5	391.3
10954	E	406.5	407.2
10955	D	390.5	391.2
10956	D	390.5	391.3
10957	E	390.5	391.3
10958	F	400.5	401.5
10961	C	484.5	485.2
10962	D	421.5	422.2
10963	E	377.4	378.2
10964	A	434.5	435.2
10965	H1	377.4	378.2
10966	H1	377.4	378.2
10968	E	376.5	377.2
10969	D	416.5	417.2
10970	H2	422.9	423.3
10971	C	391.5	392.2
10972	A	432.5	433.2
10973	D	416.5	417.2
10974	E	391.5	392.2
10975	C	442.5	443.2
10976	F	377.4	378.2

Example No	Human FXIIa IC50 (nM)	Molecular weight	LCMS Mass Ion
11001	B	406.5	407.4
12001	A	525.6	526.3
12007	A	391.5	392.2
12008	A	511.6	512.2
12009	A	433.5	434.4
12010	B	525.6	526.5
12011	C	391.5	392.4
12012	B	563.7	564.6
12013	C	449.5	450.4
12014	A	559.7	560.2
12015	A	546.0	547.3
12016	A	523.6	524.4
12017	A	524.6	525.4
12018	A	563.7	564.6
12019	A	509.6	510.4
12020	B	561.6	562.3
12021	A	526.6	527.6
12022	A	526.6	527.4
12023	A	560.0	560.3
12024	B	575.7	576.7
12025	D	534.0	534.2
12026	B	529.6	530.4
12027	B	491.6	492.4
12028	A	509.6	510.1
12031	B	545.6	546.4
12034	A	549.6	550.3
12035	A	495.6	496.3
12036	AA	510.6	510.6
12038	AA	538.6	539.6
12039	A	523.6	524.5
12040	A	548.6	549.4

Example No	Human FXIIa IC50 (nM)	Molecular weight	LCMS Mass Ion
12041	AA	538.6	539.4
12042	A	553.7	554.4
12044	A	548.6	549.7
12045	F	476.6	477.2
12046	H2	490.6	491.3
12047	A	574.7	575.4
12048	A	573.6	574.7
12049	A	558.1	558.9
12050	A	591.6	592.7
12051	A	567.6	566.4
12052	A	574.7	575.3
12053	A	602.5	604.1
12054	A	540.6	541.3
12055	A	574.7	575.1
12056	A	589.6	590.6
12057	AA	508.6	509.2
12058	A	542.6	543.7
12059	A	540.6	541.7
12060	AA	545.6	546.3
12061	AA	540.6	541.3
12062	A	554.6	555.3
12063	H2	476.6	477.3
12064	A	468.6	469.2
12065	AA	468.6	469.2
12067	A	554.6	555.3
12068	AA	528.6	529.6
12069	A	592.6	593.3
12070	A	564.6	565.4
12071	A	525.6	526.3
12072	C	542.6	543.3
13001	A	525.6	526.3

Example No	Human FXIIa IC50 (nM)	Molecular weight	LCMS Mass Ion
13002	F	606.6	607.2
13003	B	433.5	434.3
13004	B	546.0	546.3
13005	B	491.6	492.4
13006	A	511.6	512.3
13007	B	391.5	392.3
13008	C	523.6	524.3
13009	A	526.6	527.3
13010	B	524.6	525.3
13011	C	538.6	539.3
13012	A	524.6	525.4
13013	B	526.6	527.3
13014	B	559.7	560.2
13015	B	509.6	510.3
13016	C	524.6	525.3
13017	C	558.1	558.2
13018	C	508.6	509.3
13019	C	510.6	511.3
13020	A	560.0	561.3
13021	C	509.6	510.2
13022	A	529.6	530.3

Determination of related protease inhibition

In vitro inhibition of related proteases was determined using an IC_{50} assay based on standard literature methods (see e.g. Shori et al., Biochem. Pharmacol., 1992,43, 1209; Bouckaert et al., European Journal of Medicinal Chemistry 110 (2016) 181). Human serine protease enzyme Plasma Kallikrein, KLK1, FXa, Plasmin, Thrombin and Trypsin were assayed for enzymatic activity using an appropriate fluorogenic substrate at Km concentration, FXIa at fixed substrate concentration of 100µM and various concentrations of the test compound. Protease activity was measured by monitoring the accumulation of liberated fluorescence from the substrate over 5 min at 25 °C. The linear rate of fluorescence increase

per minute was expressed as percentage (%) activity. IC_{50} values were calculated as the concentration of inhibitor giving 50% inhibition of the uninhibited enzyme activity (100%).

Data acquired from this assay are shown in Table 17 using the scale shown in Table 18.

Table 17: Enzyme selectivity data

Example No	IC_{50} (human PKal) nM	IC_{50} (human KLK1) nM	IC_{50} (human plasmin) nM	IC_{50} (human FXa) nM	IC_{50} (human FXIa) nM	IC_{50} (human thrombin) nM	IC_{50} (human trypsin) nM
1001	G3	E	G3	F	G3	F	G3
1002	G3	E	G3	F	G3	F	F
1002.1	G3	E		F		E	
1002.2	G3						
1004	G3	E		D		F	
1005.1	G3						
1006	G3	D		D		F	
1009	G4	G4					
1010		G3		D			
1011	G4	F		D		F	
1012	G4	G3		D		D	
1013	G3						
1014	G3						
1015	G3						
1016	G3	E		G3		G3	
1017	G3	E		F		F	

Example No	IC_{50} (human PKal) nM	IC_{50} (human KLK1) nM	IC_{50} (human plasmin) nM	IC_{50} (human FXa) nM	IC_{50} (human FXIa) nM	IC_{50} (human thrombin) nM	IC_{50} (human trypsin) nM
1018	G3						
1019	G3	E		F		F	
1101	G3	E		D		F	
1105	G3	E		D		F	
1109	G3	D		F		F	
1113	G3						
1118	G3	E		G3		F	
1125	G3						
1126	G3						
1127	G3						
1129	G4						
1130	G3						
1131	G3						
2020	G3	E		G3		G3	
2022	G3	E		G3		G3	
2204	G3	E		G3		G3	
2205	G3	F	G3	G3		G3	G3
2206	G3						
2207	G3						

Example No	IC_{50} (human PKal) nM	IC_{50} (human KLK1) nM	IC_{50} (human plasmin) nM	IC_{50} (human FXa) nM	IC_{50} (human FXIa) nM	IC_{50} (human thrombin) nM	IC_{50} (human trypsin) nM
2208	G3						
2210	G3						
2211	G1	D		G3			
2212	F	D	G3	F		G3	F
4401	G3	D		G3		G3	
5003	G3	E		G3		G3	
6601	G3	E		F		F	
6602	G3	E	G3	F		F	G3
6605	G3	F		F		F	
6606	G3						
6608	G3	E		G3		G3	
6609	G3	E		G3		G3	
6610	G3						
6611	G3						
6612	G3						
6613		E		F			
6614	G1	E		G3			
6615		E		G3			
6616		E		G3			

Example No	IC_{50} (human PKal) nM	IC_{50} (human KLK1) nM	IC_{50} (human plasmin) nM	IC_{50} (human FXa) nM	IC_{50} (human FXIa) nM	IC_{50} (human thrombin) nM	IC_{50} (human trypsin) nM
6617	G3	E		F			
6618	G3	E	G3	F		G3	F
6619		F					
6620	G3	E	G3	G3		G3	E
6621	G3	E	G3	G3		G3	G3
6622		D					
6624	F	D	G3	D		G3	F
6626		D					
6627		E					
6628		E					
6629	G3	D	F	G3		G3	F
7703	G3						
7704	G3						
8801	G3						
8803	G3						
8804	G3						
8805	G3						
8806	G3	F	G3	G3		G3	G3
8807		F					

Example No	IC_{50} (human PKal) nM	IC_{50} (human KLK1) nM	IC_{50} (human plasmin) nM	IC_{50} (human FXa) nM	IC_{50} (human FXIa) nM	IC_{50} (human thrombin) nM	IC_{50} (human trypsin) nM
8808	G3						
9001	G3						
9002	G3						
9003	G3						
10901	G3	E		F		F	
10903	G1						
10904	G3	E		G3		F	
10906	G3	F	G3	G3		G3	F
10907	G3	G3		G3		G3	
10908	G3						
10909	G3						
10910	G3						
10911	G3						
10912	G3						
10914	G3						
10915	G3						
10918	G3	G4		G3			
10919	G3	G4		G3			
10920	E	E		F			

Example No	IC_{50} (human PKal) nM	IC_{50} (human KLK1) nM	IC_{50} (human plasmin) nM	IC_{50} (human FXa) nM	IC_{50} (human FXIa) nM	IC_{50} (human thrombin) nM	IC_{50} (human trypsin) nM
10921		F					
10922		C					
10923		C					
10924		E					
10925		E					
10926	G3	E	G3	G3		G3	E
10928	G3	F	G3	F		G3	F
10940	G3	F	G3	G3		G3	F
10942		E		G3			
11001	G3	F	G3	G3		G3	F
12001	G3	E		G3		G3	
12007	G1	F		G3			
12008	G1	D		G3			
12009	G1	F		G3			
12010		A					
12017	F	E	F	F		G3	G3
12019	G3	D	G3	G3		G3	G3
12036	F	D	E	F		G3	G3
12038	E	E	F	D		G3	F

Example No	IC_{50} (human PKal) nM	IC_{50} (human KLK1) nM	IC_{50} (human plasmin) nM	IC_{50} (human FXa) nM	IC_{50} (human FXIa) nM	IC_{50} (human thrombin) nM	IC_{50} (human trypsin) nM
13001	G3	G1		G1			
13002	G3						

Table 18: Scale used to present enzyme selectivity data

Category	IC_{50} (nM)
A	10 - 100
B	100 - 300
C	300 – 1,000
D	1,000 – 3,000
E	3,000 – 10,000
F	10,000 – 40,000
G1	>4,000
G2	>20,000
G3	>40,000
G4	>100,000

Pharmacokinetics

Pharmacokinetic studies of the compounds in Table 19 were performed to assess the pharmacokinetics following a single intravenous dose and a single oral dose in male Sprague-Dawley rats. Two rats were given a single intravenous dose of 1 mL/kg of a nominal 1 mg/mL (1 mg/kg) composition of test compound in 10% DMSO / 10% Cremophor EL / 80% SWFI vehicle. Two rats were given a single oral dose of 5 mL/kg of a nominal 1 mg/mL (5 mg/kg) composition of test compound in 10% DMSO / 10% Cremophor EL / 80% SWFI vehicle.

Following intravenous dosing, blood samples were collected over a period of 12 h. Sample times were 2, 5, 15 and 30 min then 1, 2, 4, 6, and 12 h. Following oral dosing, blood samples were collected over a period of 24 h. Sample times were 5, 15 and 30 min then 1, 2, 4, 6, 8, 12 and 24 h.

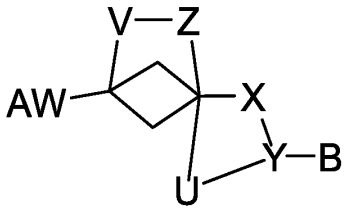
Following collection, blood samples were centrifuged and the plasma fraction analysed for concentration of test compound by LCMS. Oral bioavailability and half-life calculations from these studies were obtained using Phoenix WinNonlin (v8.0) and are shown below:

Table 19: Oral exposure data

Example No	Dose iv (mg/kg)	Dose po (mg/kg)	F%	$T_{1/2}$ (min)
1001	0.88	4.45	30.4%	469.5
1002.1	1.1	5.7	41.0%	441.3
2020	1.0	5.3	19.9%	632.1
2022	1.06	5.3	42.6%	188.0
6602	1.11	5.7	33.5%	342.2
6624	1.04	5.2	14.8%	398.1
10901	0.95	4.8	9.3%	715.3
10906	0.54	2.7	40.5%	152.9
12001	1.59	8.1	8.2%	68.2
12016	0.48	5.2	0.4%	64.8

Claims

1. A compound of formula (I),



Formula (I),

wherein:

U is absent -C(R16)(R17)-, $CH_2C(R16)(R17)$ or $C(R16)(R17)CH_2$;

-V-Z- is:

absent, $-CH_2-$, or $-CH_2-O-CH_2$; or

V is selected from CH_2, O and NR18, and Z is selected from $-C(R16)(R17)-CH_2-$ and -C(R16)(R17)-;

or,

V is selected from $-CH_2-C(R16)(R17)-$ and -C(R16)(R17)-, and Z is selected from CH_2, O and NR18;

wherein R18 is selected from H, alkyl, $(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), C(=O)SR19 and SO_2R19;

wherein R19 is selected from alkyl, cycloalkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a];

X is selected from a bond, O, CR1R2, C=O and NR12;

Y is, where possible, selected from O, CR1R2, CR1, C=O, N and NR12;

R1 is selected from H, alkyl, alkoxy, OH, halo and NR13R14;

R2 is selected from H and small alkyl;

wherein when one of X or Y is C=O, the other is, where possible, O, CR1R2, CR1, N or NR12;

wherein when X is NR12, Y is, where possible, CR1R2, CR1 or C=O;

wherein when Y is, where possible, NR12 or N, X is a bond, CR1R2 or C=O;

wherein when X is O, Y is, where possible, CR1R2, CR1 or C=O;

wherein when Y, where possible, is O, X is a bond, CR1R2 or C=O;

wherein when X is a bond, Y is, where possible, O, N or NR12;

wherein when U is not absent, -V-Z- is absent;

wherein when -V-Z- is not absent, U is absent;

B is selected from:

(i) heteroaryl[a];

(ii) aryl;

(iii) a 5- to 6- membered non-aromatic heterocyclic ring containing one N ring member, which is unsaturated with 1 or 2 double bonds, wherein the non-aromatic heterocyclic ring is optionally substituted by 1, 2 or 3 substituents independently selected from alkyl, alkoxy, aryl[b], OH, OCF_3, halo, oxo, CN, and CF_3; and

(iv) a fused 5,5-, 6,5- or 6,6- bicyclic ring containing an aromatic ring fused to a non-aromatic ring, wherein the bicyclic ring optionally contains one or two N ring members, wherein the fused 5,5-, 6,5- or 6,6- bicyclic ring may be optionally substituted with 1, 2, or 3 substituted by up to three substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, oxo, CN, and CF_3, wherein the 6,5- bicyclic ring may be attached via the 6- or 5- membered ring;

AW- is selected from:

$-(CH_2)_{0-6}$-(CHR15)-$(CH_2)_{0-6}$-A, -(CHR12)-A, -O-(CHR12)-A, $-(CH_2)_{0-6}$-A, $-(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A, $-(CH_2)_{0-6}$-NH-$(CH_2)_{0-6}$-A, $-(CH_2)_{0-6}$-NR12-$(CH_2)_{1-6}$-C(=O)-A, $-(CH_2)_{0-6}$-NH-C(=O)-$(CH_2)_{0-6}$-A, -C(=O)NR12-$(CH_2)_{0-6}$-A, $-(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A, $-(CH_2)_{0-6}$-(phenyl)-$(CH_2)_{0-6}$-A, -NH-SO_2-A and -SO_2-NH-A;

A is a 4- to 15- membered mono-, bi-, or tri- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, $-(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN;

wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro;

wherein when A is a tricyclic ring system, each of the three rings in the tricyclic ring system is either fused, bridged or spiro to at least one of the other rings in the tricyclic ring system;

wherein when -V-Z- is $-CH_2$-, U is absent, and AW- is A-(C=O)-, A may not be substituted by $-(CH_2)_0$-heteroaryl;

alkyl is a linear saturated hydrocarbon having up to 10 carbon atoms (C_1-C_{10}) or a branched saturated hydrocarbon of between 3 and 10 carbon atoms (C_3-C_{10}); alkyl may optionally be substituted with 1, 2 or 3 substituents independently selected from (C_1-C_6)alkoxy, OH, -NR13R14, -C(=O)OR13, -C(=O)NR13R14, CN, CF_3, halo;

alkyl^b is a linear saturated hydrocarbon having up to 10 carbon atoms (C_1-C_{10}) or a branched saturated hydrocarbon of between 3 and 10 carbon atoms (C_3-C_{10}); alkyl^b may optionally be substituted with 1, 2 or 3 substituents independently selected from (C_1-C_6)alkoxy, OH, CN, CF_3, halo;

small alkyl is a linear saturated hydrocarbon having up to 4 carbon atoms (C_1-C_4) or a branched saturated hydrocarbon of between 3 and 4 carbon atoms (C_3-C_4); small alkyl may optionally be substituted with 1 or 2 substituents independently selected from (C1-C6)alkoxy, OH, NR13R14, C(=O)OR13, C(=O)NR13R14, CN, CF_3, halo;

aryl is phenyl, biphenyl or naphthyl; aryl may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, methylenedioxy, ethylenedioxy, OH, halo, CN, -$(CH_2)_{0-3}$-O-heteroaryl^a, aryl^b, -O-aryl^b, -$(CH_2)_{1-3}$-aryl^b, -$(CH_2)_{0-3}$-heteroaryl^a, -C(=O)OR13, -C(=O)NR13R14, -$(CH_2)_{0-3}$-NR13R14, OCF_3 and CF_3;

aryl^b is phenyl, biphenyl or naphthyl; aryl^b may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl^b, alkoxy, OH, halo, CN, and CF_3;

cycloalkyl is a monocyclic saturated hydrocarbon ring of between 3 and 6 carbon atoms (C_3-C_6); cycloalkyl may optionally be substituted with 1 or 2 substituents independently selected from alkyl, (C_1-C_6)alkoxy, OH, CN, CF_3, halo;

alkoxy is a linear O-linked hydrocarbon of between 1 and 6 carbon atoms (C_1-C_6) or a branched O-linked hydrocarbon of between 3 and 6 carbon atoms (C_3-C_6); alkoxy may optionally be substituted with 1 or 2 substituents independently selected from OH, CN, CF_3, and fluoro;

halo is F, Cl, Br, or I;

heteroaryl is a 5- or 6- membered carbon-containing aromatic ring containing one, two or three ring members that are selected from N, NR8, S, and O; heteroaryl may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, CN, and CF_3;

heteroaryl[a] is a 5, 6, 9 or 10 membered mono- or bi-cyclic aromatic ring, containing, where possible, 1, 2, 3 or 4 ring members independently selected from N, NR12, S and O; heteroaryl[a] may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl, alkoxy, OH, OCF_3, halo, CN, aryl[b], $-(CH_2)_{0-3}$-NR13R14, heteroaryl[b], -C(=O)OR12, -C(=O)NR13R14 and CF_3;

heteroaryl[b] is a 5, 6, 9 or 10 membered mono- or bi-cyclic aromatic ring, containing, where possible, 1, 2 or 3 ring members independently selected from N, NR12, S and O; wherein heteroaryl[b] may be optionally substituted with 1, 2 or 3 substituents independently selected from alkyl[b], alkoxy, OH, halo, CN, aryl[b], $-(CH_2)_{1-3}$-aryl[b], and CF_3;

R8 is independently selected from H, alkyl, cycloalkyl, and heterocycloalkyl;

heterocycloalkyl is a non-aromatic carbon-containing monocyclic ring containing 3, 4, 5, or 6, ring members, wherein at least one ring member is independently selected from N, NR12, S, and O; heterocycloalkyl may be optionally be substituted with 1 or 2 substituents independently selected from alkyl, $(C_1$-$C_6)$alkoxy, OH, CN, CF_3, halo;

R12 is independently selected from H, alkyl, and cycloalkyl;

R13 and R14 are independently selected from H, alkyl[b], aryl[b] and heteroaryl[b] or R13 and R14 together with the nitrogen atom to which they are attached form a carbon-containing 4-, 5-, 6- or 7-membered heterocyclic ring, optionally containing an additional heteroatom selected from N, NR12, S, SO, SO_2, and O, which may be saturated or unsaturated with 1 or 2 double bonds and which may be optionally mono- or di-substituted with substituents selected from oxo, alkyl[b], alkoxy, OH, halo and CF_3;

R15 is selected from alkyl, halo, CF_3, CN, OH, alkoxy, NR13R14, and CONR13R14;

R16 and R17 are independently selected from H and small alkyl;

and tautomers, isomers, stereoisomers (including enantiomers, diastereoisomers and racemic and scalemic mixtures thereof), deuterated isotopes, and pharmaceutically acceptable salts and/or solvates thereof;

wherein the compound is not *N*-(2-chlorophenyl)-3-((5-cyano-1*H*-indazol-1-yl)-methyl)-*N*-methylbicyclo-[1.1.1]pentane-1-carboxamide.

2. A compound of formula (I) according to claim 1, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein, when not absent, -V-Z- is selected from:
$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-CH_2-O-$, $-CH_2-CH_2-CH_2-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$; or
when -V-Z- is absent:
U is absent, CH_2 or $-CH_2CH_2-$.

3. A compound of formula (I) according to claim 1, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein, when not absent, -V-Z- is selected from:
$-CH_2-$, $-O-CH_2-$, $-O-C(CH_3)_2-$, $-CH_2-O-$, $-C(CH_3)_2-O-$, $-NH-CH_2-$, $-CH_2-NH-$, $-N(COCH_3)-CH_2$, $-CH_2-N(COCH_3)$, $-CH_2-CH_2-$, $-O-CH_2-CH_2$, $-CH_2-O-CH_2$, $-CH_2-CH_2-O-$, and $-CH_2-CH_2-CH_2-$; or,
wherein when -V-Z- is absent:
U is absent, CH_2 or $-CH_2CH_2-$.

4. A compound of formula (I) according to claims 2 to 3, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein -V-Z- is selected from $-CH_2-$, $-O-CH_2-$, $-CH_2-O-$, $-CH_2-CH_2-O-$, $-CH_2-N(R18)-$ and $-N(R18)-CH_2-$
wherein R18 is selected from:
$(CH_2)_{0-6}$-aryl, $(CH_2)_{0-6}$-heteroaryl[a], C(=O)R19, C(=O)OR19, C(=O)NHR19, C(=O)N(alkyl)(R19), and SO_2R19;
wherein R19 is selected from alkyl, $(CH_2)_{0-6}$-aryl and $(CH_2)_{0-6}$-heteroaryl[a]; or
when -V-Z- is absent:

U is absent, CH_2 or $-CH_2CH_2-$.

5. A compound of formula (I) according to claims 2 to 4, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein -V-Z- is selected from $-CH_2-$, $-O-CH_2-$, $-CH_2-O-$ and $-CH_2-CH_2-O-$.

6. A compound of formula (I) according to any of claims 1 to 5, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein X is selected from a bond and CR1R2.

7. A compound of formula (I) according to claim 6, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein X is CH_2.

8. A compound of formula (I) according to any preceding claim, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein Y is, where possible, selected from O, CR1R2, N and NR12.

9. A compound of formula (I) according to claim 8, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein Y is, where possible, selected from N and NR12.

10. A compound of formula (I) according to claim 9, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein Y is, where possible, selected from N and NH.

11. A compound of formula (I) according to any of claims 1 to 9, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein Y is, where possible, NR12.

12. A compound of formula (I) according to claim 11, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein Y is NH.

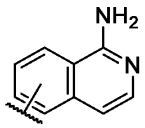
13. A compound of formula (I) according to any preceding claim, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein B is selected from heteroaryl[a] and aryl.

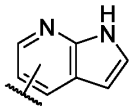
14. A compound of formula (I) according to claim 13, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein B is heteroaryl[a].

15. A compound of formula (I) according to claim 14, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein B is a 9 or 10 membered bicyclic aromatic ring, containing 1 or 2 ring members independently selected from N or NR12, optionally substituted as for hereroaryl[a].

16. A compound of formula (I) according to claim 15, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein B is:
isoquinolinyl, optionally substituted as for heteroaryl[a], or
azaindole, optionally substituted as for heteroaryl[a].

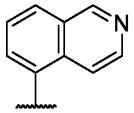
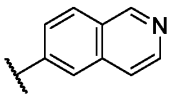
17. A compound of formula (I) according to claim 16, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein B is selected from:

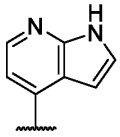
isoquinolinyl, substituted with NH_2 at the 1- position  , optionally further substituted with 1 or 2 substituents as for heteroaryl[a]; and

7-azaindolyl  , optionally substituted as for heteroaryl[a].

18. A compound of formula (I) according to claim 16, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

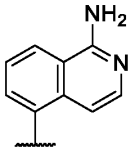
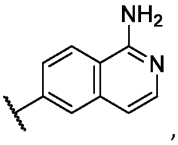
wherein B is selected from:

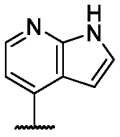
isoquinolinyl, selected from  and  , optionally substituted as for heteroaryl[a]; and

7-azaindolyl  optionally substituted as for heteroaryl[a].

19. A compound of formula (I) according to claim 17, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein B is selected from:

isoquinolinyl, substituted with NH_2 at the 1- position, selected from  and  , optionally further substituted with 1 or 2 substituents as for heteroaryl[a]; and

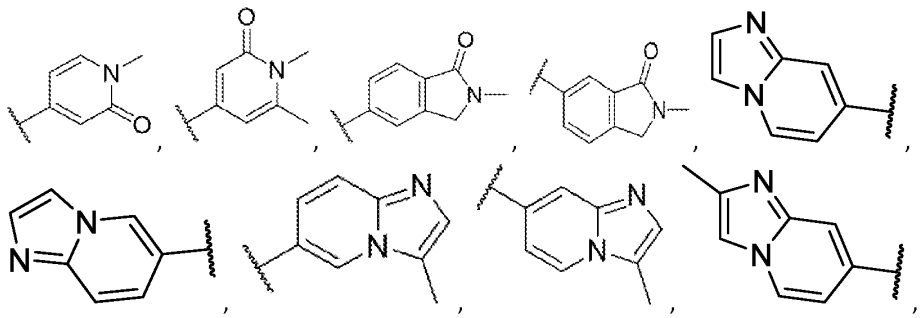
7-azaindolyl  , optionally substituted as for heteroaryl[a].

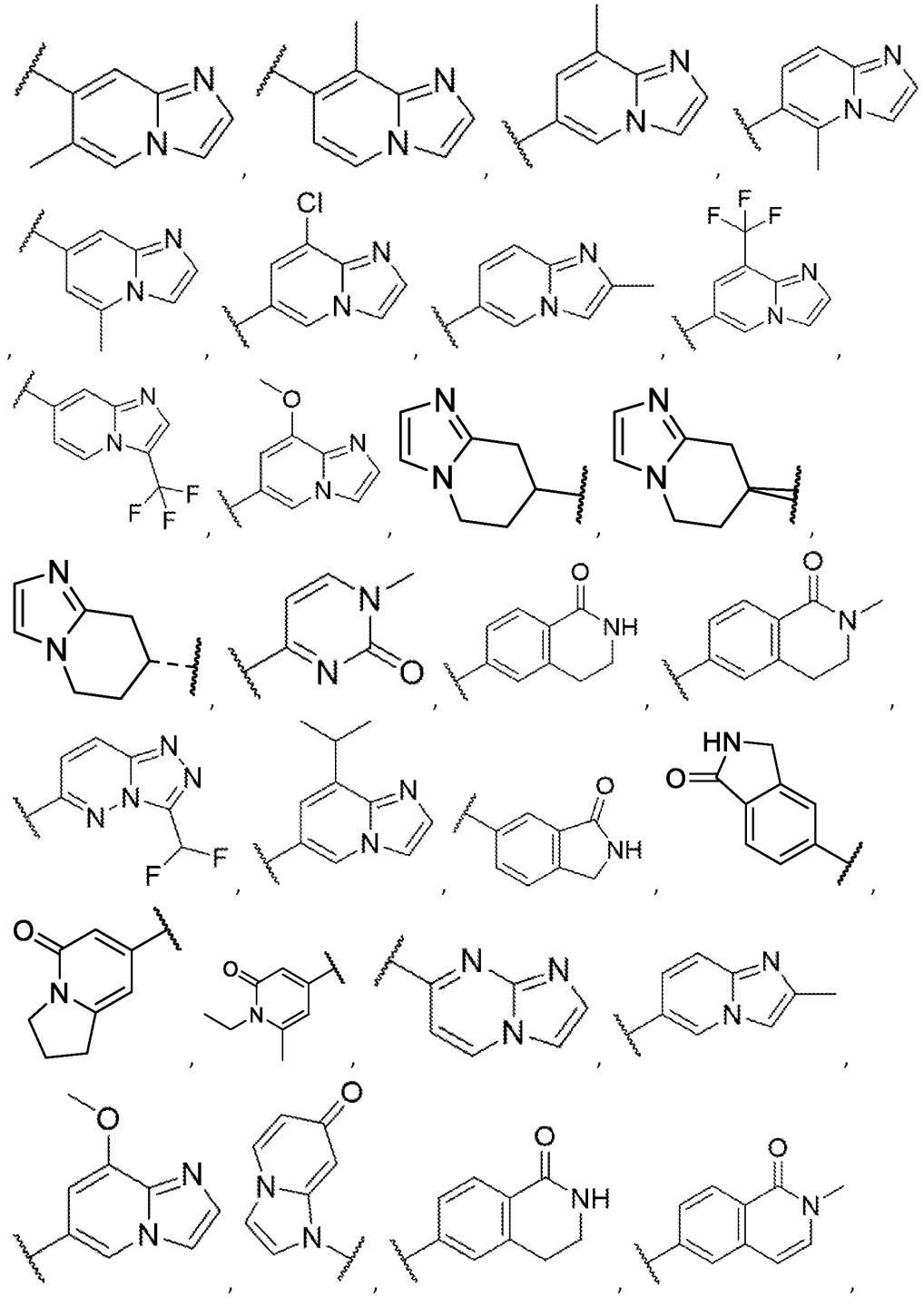
20. A compound of formula (I) according to any preceding claim, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein AW- is selected from -(CHR12)-A, -$(CH_2)_{0-6}$-C(=O)-$(CH_2)_{0-6}$-A, and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A.

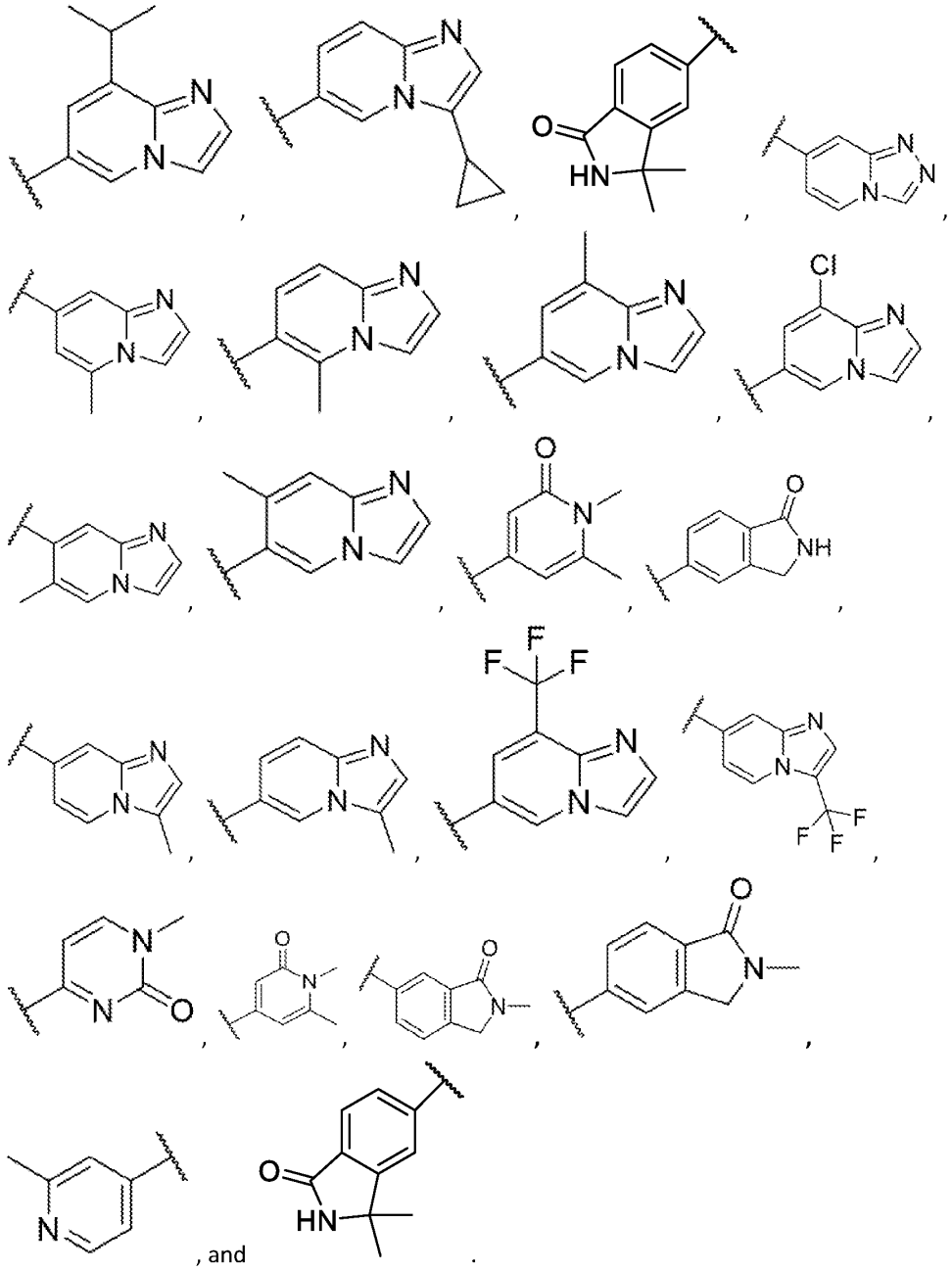
21. A compound of formula (I) according to claim 20, or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein AW- is selected from -(CHR12)-A, and -$(CH_2)_{0-6}$-O-$(CH_2)_{0-6}$-A.

22. A compound of formula (I) according to any preceding claim or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein A is a 4- to 12- membered mono- or bi- cyclic ring system, containing one N ring member and optionally one, two or three further ring members independently selected from N, O and S, optionally wherein the ring system is substituted, where possible, with 1, 2, 3 or 4 substituents independently selected from halo, alkyl, OH, oxo, cycloalkyl, alkoxy, -$(CH_2)_{0-2}$-heteroaryl, heterocycloalkyl, C(=O)R12, C(=O)OR13, C(=O)NR13R14, NR13R14, CF_3, CN;
wherein when A is a bicyclic ring system, the bicyclic ring system is fused, bridged or spiro.

23. A compound of formula (I) according to claim 22 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,
wherein A is selected from:



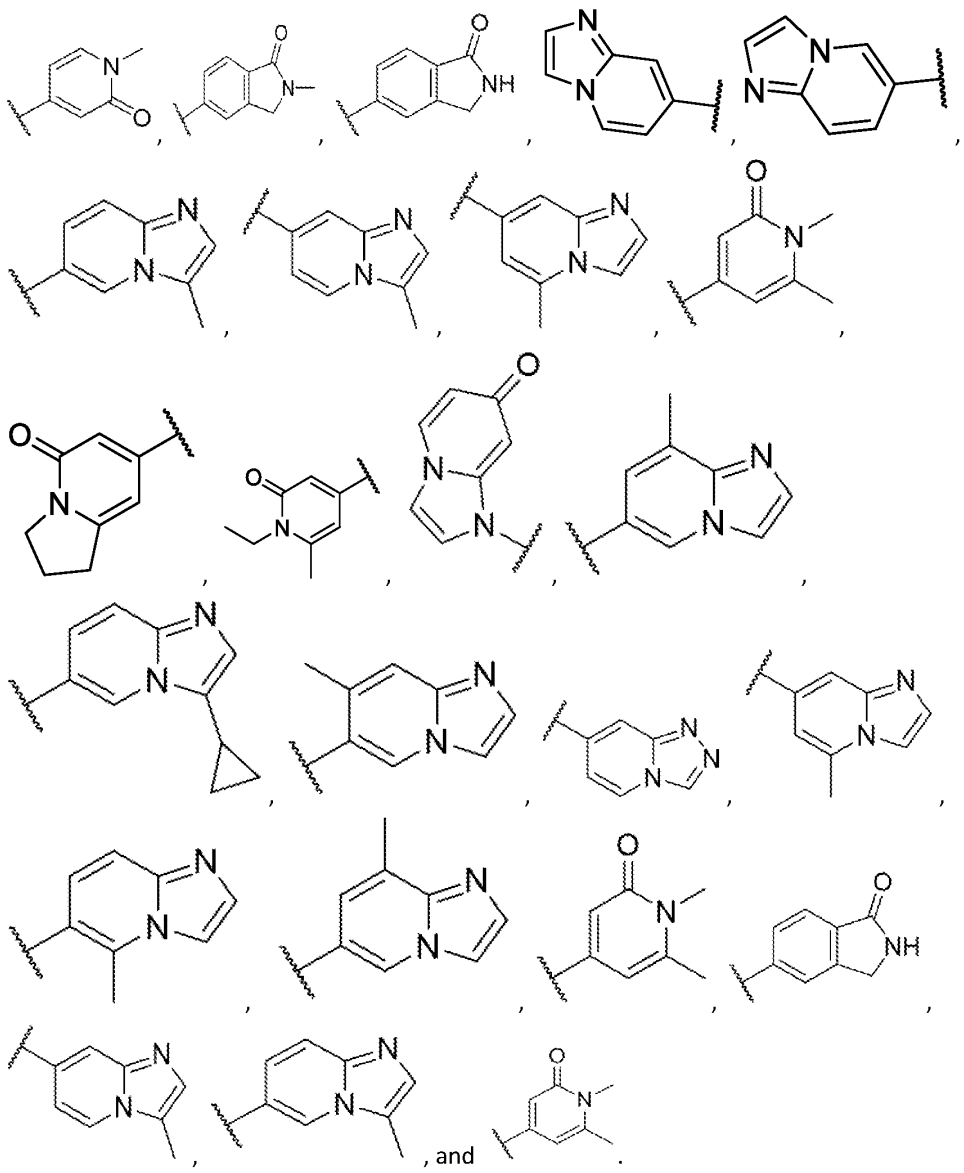




, and .

24. A compound of formula (I) according to claim 22 or a tautomer, isomer, stereoisomer (including an enantiomer, a diastereoisomer and a racemic and scalemic mixture thereof), a deuterated isotope, and a pharmaceutically acceptable salt and/or solvate thereof,

wherein A is selected from:



25. A compound selected from Table 1a, Table 1b, Table 2a, Table 2b, Table 3a, Table 4a, Table 5b, Table 6a, Table 6b, Table 7a, Table 7b, Table 8a, Table 8b, Table 9b, Table 10a, Table 10b, Table 11b, Table 12b, or Table 13b, or a pharmaceutically acceptable salt, solvate, or solvate of a salt thereof.

26. A pharmaceutical composition comprising: a compound, or a pharmaceutically acceptable salt and/or solvate thereof, according to any of claims 1 to 25, and at least one pharmaceutically acceptable excipient.

27. A compound, or a pharmaceutically acceptable salt and/or solvate thereof, as defined in any of claims 1 to 25, or the pharmaceutical composition according to claim 26, for use in medicine.

28. A compound, or a pharmaceutically acceptable salt and/or solvate thereof, as defined in any of claims 1 to 25, or the pharmaceutical composition according to claim 26, for use in a method of treatment of a disease or condition in which Factor XIIa activity is implicated; wherein the disease or condition in which Factor XIIa activity is implicated is a bradykinin-mediated angioedema, wherein the bradykinin-mediated angioedema is hereditary angioedema.

29. A compound, or a pharmaceutically acceptable salt and/or solvate thereof, as defined in any of claims 1 to 25, or the pharmaceutical composition according to claim 26, for use in a method of treatment of a disease or condition in which Factor XIIa activity is implicated; wherein the disease or condition in which Factor XIIa activity is implicated is a bradykinin-mediated angioedema, wherein the bradykinin-mediated angioedema is non hereditary.

30. A compound, or a pharmaceutically acceptable salt and/or solvate thereof, as defined in any of claims 1 to 25, or the pharmaceutical composition according to claim 26, for use in a method of treatment of a disease or condition in which Factor XIIa activity is implicated; wherein the disease or condition in which Factor XIIa activity is implicated is a thrombotic disorder.