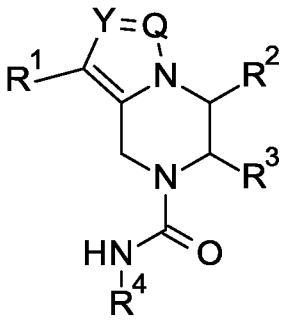
Pyrazine Compounds for the Treatment of Infectious Diseases

The present invention relates to organic compounds useful for therapy and/or prophylaxis in a mammal, and in particular for treating hepatitis B virus infection, and their pharmaceutical activity, manufacture, pharmaceutical compositions containing them and their potential use as medicaments.

FIELD OF THE INVENTION

The present invention relates to compounds of the formula (I),



(I),

or pharmaceutically acceptable salts, enantiomer or diastereomer thereof, wherein R^1 to R^4, Y and Q are as described below.The compounds of this invention are useful for the treatment or prophylaxis of hepatitis B virus infection.

Hepatitis B virus (HBV) infection is a major public health problem worldwide, roughly 30% of the world's population show serological evidence of current or past infection. Despite the introduction of a safe and effective prophylactic vaccine against the virus in the early 1980s, it is estimated that there are still more than 240 million chronic HBV carriers worldwide, a high percentage of whom will eventually develop liver cirrhosis or hepatocellular carcinoma (HCC) (WHO Hepatitis B. Fact Sheet N°204). In the 2010 Global Burden of Disease study (R Lozano, et al. Lancet, 380 (2012), 2095–2128), HBV infection ranked in the top health priorities in the world, and was the tenth leading cause of death (780,000 deaths per year). Recent studies have shown that progression to liver cirrhosis and HCC in patients with chronic HBV infection is

significantly associated with circulating HBV DNA levels. Thus, antiviral therapy against HBV is critical to prevent the progression to cirrhosis or development of HCC.

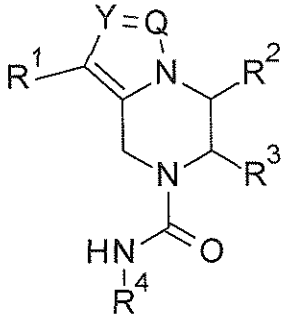
HBV is a small, enveloped virus that belongs to the Hepadnaviridae family. It contains a partly double-stranded DNA genome with approximately 3200 base pairs. HBV have a strong preference for infecting human hepatocytes. The life cycle begins when HBV attaches to the host cell membrane via its envelope proteins. The precise mechanism of viral entry has not been fully elucidated. The viral relaxed circular DNA (rcDNA) containing nucleocapsids are released into the cytoplasm and transported to the nucleus. In the nucleus, the rcDNA is repaired by both viral and cellular enzymes to form covalently closed circular DNA (cccDNA). There is evidence that each infected cell contains 1-50 cccDNA molecules as unique episomal minichromosomes. Both subgenomic RNA (sgRNA) and pregenomic RNA (pgRNA) are transcribed from the cccDNA using the cellular transcriptional machinery. After nuclear export, the pgRNA is translated into the core protein and the viral polymerase. The sgRNA is translated into the regulatory X protein and the three envelope proteins. Self-assembly of the RNA-containing viral nucleocapsid takes place via complex formation of the pgRNA with the core protein and the polymerase. Inside the nucleocapsid, the pgRNA is reverse transcribed into negative-strand DNA. rcDNA is then generated by plus-strand synthesis from the negative-strand DNA. The nucleocapsids are either re-imported to the nucleus for cccDNA amplification or enveloped and released via the endoplasmic reticulum (ER). The reverse transcriptase lacks proofreading activity; thus, mutations of the viral genome are frequent and result in the coexistence of genetically distinct viral species in infected individuals (quasispecies).

Currently, seven treatments are approved for chronic hepatitis B (CHB), including two formulations of interferon (IFN) (conventional IFN and PEG-IFN) and five nucleos(t)ide analogues (NUCs: lamivudine, adefovir dipivoxil, entecavir, telbivudine, and tenofovir disoproxil). The main difference between immunomodulatory agents and NUCs is that PEG-IFN has the advantage of a finite duration of use, whereas the use of NUCs is indefinite. The major drawback of PEG-IFN is its high frequency of adverse events. Some viral genotypes do not show good responses to interferon therapy. Long-term use of NUCs, on the other hand, poses the risk of drug resistance. The ultimate goal of antiviral therapy for CHB is to prevent progression to cirrhosis or HCC via eradication of HBV or persistent viral suppression. The majority of currently treated patients fail to achieve this goal. As indicated above, nucleocapsid assembly is a critical step for HBV genome replication. As the synthesis of viral DNA takes place

exclusively within the nucleocapsid, the assembly and disassembly of nucleocapsid must be precisely regulated to ensure correct packaging and release of the viral genome. Nucleocapsid assembly is an evolutionary constraint process that limits the diversity of HBV, and it is highly sensitive to even subtle molecular disturbances. Both assembly and disassembly of nucleocapsid make the process an attractive therapeutic target for the development of new antiviral therapies against various HBV genotypes and drug resistance isolates. A few capsid related anti-HBV compounds have been reported. For example, heteroaryldihydropyrimidines (HAP), including compounds named Bay 41-4109, Bay 38-7690 and Bay 39-5493 (Deres K. et al. Science 2003, 893), and phenylpropenamide derivatives such as AT-61 and AT-130 (Feld J. et al. Antiviral Research 2007, 168-177). Capsid has become a promising drug target with several molecules under clinical stage. There is still a need to develop new treatments for the prophylaxis and treatment of hepatitis B virus infection.

SUMMARY

The present disclosure, in one aspect, relates to novel compounds of formula (I),



(I),

wherein

R^1 is heterocyclyl, said heterocyclyl being unsubstituted or substituted with one, two or three substituents independently selected from $(C_{1-6}alkyl)_2$aminocarbonyl, $(C_{1-6}alkyl)_2$morpholinylcarbonyl, C_{1-6}alkoxy, C_{1-6}alkoxyC_{1-6}alkyl, C_{1-6}alkoxycarbonyl, C_{1-6}alkyl, C_{1-6}alkyl(C_{1-6}alkylsulfonyl)amino, C_{1-6}alkylaminocarbonyl, C_{1-6}alkylcarbonyl, C_{1-6}alkylcarbonylamino, C_{1-6}alkylimidazolyl, C_{1-6}alkylmorpholinylcarbonyl, C_{1-6}alkyloxadiazolyl, C_{1-6}alkyloxazolyl, C_{1-6}alkylpyrazolyl, C_{1-6}alkylsulfonyl, C_{1-6}alkylsulfonylamino, C_{1-6}alkylsulfonylC_{1-6}alkyl, carbamoyl, cyano, dioxopyrrolidinyl, haloC_{1-6}alkyl, haloC_{1-6}alkyloxadiazolyl, halogen, halopiperidinylcarbonyl, halopyridinyl, halopyrimidinylamino, halopyrimidinyloxy, halopyrrolidinylcarbonyl, hydroxy, hydroxyazetidinylcarbonyl, hydroxyC_{1-6}alkyl, hydroxyC_{1-6}alkyl(C_{1-}

$_6$alkyl)aminocarbonyl, hydroxyC_{1-6}alkylaminocarbonyl, hydroxypyrrolidinylcarbonyl, morpholinylcarbonyl, oxadiazolyl, oxazolyl, oxazolylaminocarbonyl, oxazolyl(C_{1-6}alkyl)aminocarbonyl, oxazolylcarbonyl, oxazolylcarbonyl(C_{1-6}alkyl)amino, oxomorpholinyl, oxooxazolidinyl, oxopyrrolidinyl, phenyl, phenylcarbonyl, pyrazolylC_{1-6}alkyl, pyridinyl, pyrimidinyl, pyrimidinylamino, pyrimidinyl(C_{1-6}alkyl)amino, pyrimidinyloxy, pyrimidinyloxyC_{1-6}alkyl, pyrrolidinylcarbonyl and thiazolyl;

heteroaryl, said heteroaryl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, C_{1-6}alkyl ,haloC_{1-6}alkyl, hydroxy C_{1-6}alkyl and C_{1-6}alkoxyC_{1-6}alkyl;

phenyl, said phenyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, hydroxy, C_{1-6}alkyl, C_{1-6}alkoxy, C_{3-7}cycloalkyl, haloC_{1-6}alkoxy and haloC_{1-6}alkyl; or

C_{3-7}cycloalkyl;

R^2 and R^3 are independently selected from hydrogen and C_{1-6}alkyl;

R^4 is heteroaryl, said heteroaryl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, C_{1-6}alkyl, haloC_{1-6}alkyl, C_{1-6}alkoxy, C_{3-7}cycloalkyl and $(C_{1-6}alkyl)_2$amino;

aryl, said aryl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, C_{3-7}cycloalkyl, C_{1-6}alkyl, C_{2-6}alkynyl, C_{1-6}alkoxy, haloC_{1-6}alkyl and haloC_{1-6}alkoxy;

phenylC_{1-6}alkyl, said phenylC_{1-6}alkyl being unsubstituted or substituted with one, two or three halogen; or

C_{3-7}cycloalkyl;

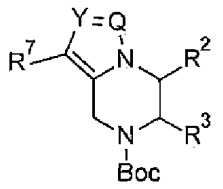
Y and Q are independently selected from CH and N;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

Objects of the embodiments disclosed herein are novel compounds of formula (I), their manufacture, medicaments based on a compound in accordance with the invention and their production as well as the use of compounds of formula (I) as HBV inhibitors and for the treatment or prophylaxis of HBV infection.

In another aspect, there is provided a process for the preparation of a compound as defined herein comprising any of the following steps:

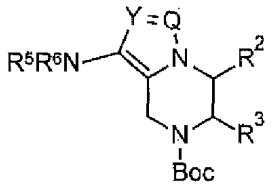
(a) a reaction of a compound of formula (V),



(V),

with an acid followed by urea formation with amine R^4NH_2 in the presence of a phosgene equivalent;

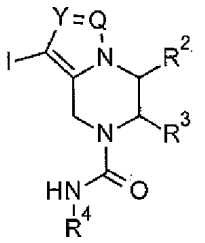
(b) a reaction of a compound of formula (VII),



(VII),

with an acid followed by urea formation with amine R^4NH_2 in the presence of a phosgene equivalent;

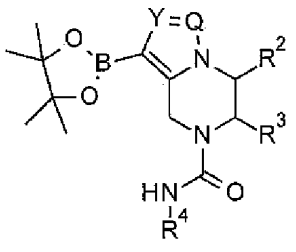
(c) a reaction of a compound of formula (IX),



(IX),

with R^7-$B(OH)_2$; or

(d) a reaction of a compound of formula (X),



(X),

with halide via Suzuki-Miyaura reaction;

wherein R^2, R^3 , R^4 are as defined herein;

R^5 and R^6 together with the nitrogen atom they are attached to form a 3-7 membered heterocyclyl; and

R^7 is aryl or heteroaryl.

In another aspect, there is provided a compound or pharmaceutically acceptable salts, enantiomers or diastereomers as defined herein for use as therapeutically active substance.

In another aspect, there is provided a pharmaceutical composition comprising a compound as defined herein and a therapeutically inert carrier.

In another aspect, there is provided use of a compound as defined herein for the preparation of a medicament for the treatment or prophylaxis of hepatitis B virus infection.

In another aspect, there is provided a compound or pharmaceutically acceptable salt, enantiomer or diastereomer as defined herein for use in the treatment or prophylaxis of hepatitis B virus infection.

In another aspect, there is provided a compound or pharmaceutically acceptable salt, enantiomer or diastereomer as defined herein, when manufactured according to a process as defined herein.

DETAILED DESCRIPTION OF THE INVENTION

DEFINITIONS

The term "C_{1-6}alkyl" denotes a monovalent linear or branched saturated hydrocarbon group of 1 to 6 carbon atoms. In particular embodiments, C_{1-6}alkyl has 1 to 6 carbon atoms, and in more particular embodiments 1 to 4 carbon atoms. Examples of C_{1-6}alkyl include methyl, ethyl, propyl, isopropyl, n-butyl, iso-butyl, sec-butyl or tert-butyl.

The term "halo" or "halogen" are used interchangeably herein and denote fluoro, chloro, bromo or iodo.

The term "haloC_{1-6}alkyl" denotes a C_{1-6}alkyl group wherein at least one of the hydrogen atoms of the C_{1-6}alkyl group has been replaced by same or different halogen atoms, particularly fluoro atoms. Examples of haloC_{1-6}alkyl include monofluoro-, difluoro- or trifluoro-methyl, -ethyl or -propyl, for example 3,3,3-trifluoropropyl, 2-fluoroethyl, trifluoroethyl, fluoromethyl, difluoromethyl, difluoroethyl or trifluoromethyl.

The term "haloC_{1-6}alkoxy" denotes a C_{1-6}alkoxy group wherein at least one of the hydrogen atoms of the C_{1-6}alkoxy group has been replaced by same or different halogen atoms, particularly fluoro atoms. Examples of haloC_{1-6}alkoxy include monofluoro-, difluoro- or trifluoro-methoxy, -ethoxy or -propoxy, for example 3,3,3-trifluoropropoxy, 2-fluoroethoxy, trifluoroethoxy, fluoromethoxy, difluoromethoxy, difluoroethoxy or trifluoromethoxy.

The term "halopyridinyl" denotes a pyridinyl substituted once, twice or three times by halogen. Examples of halopyridinyl include, but not limited to, bromopyridinyl, chloropyridinyl, difluoropyridinyl, fluoropyridinyl and fluorochloropyridinyl.

The term "halopyrimidinyl" denotes a pyrimidinyl substituted once, twice or three times by halogen. Examples of halopyrimidinyl include, but not limited to, fluoropyrimidinyl.

The term "halopyrrolidinyl" denotes a pyrrolidinyl substituted once, twice or three times by halogen. Examples of halopyrrolidinyl include, but not limited to, difluoropyrrolidinyl.

The term "halopiperidinyl" denotes a piperidinyl substituted once, twice or three times by halogen. Examples of halopiperidinyl include, but not limited to, difluoropiperidinyl.

The term "pyrimidinyloxy" denotes pyrimidinyl-O-.

The term "halopyrimidinyloxy" denotes halopyrimidinyl-O-, wherein halopyrimidinyl is defined above. Examples of halopyrimidinyloxy include, but not limited to, fluoropyrimidinyloxy.

The term "oxo" denotes a divalent oxygen atom =O.

The term "heteroaryl" denotes a monovalent aromatic heterocyclic mono- or bicyclic ring system of 5 to 12 ring atoms, comprising 1, 2, 3 or 4 heteroatoms selected from N, O and S, the remaining ring atoms being carbon. Examples of heteroaryl moieties include, but not limited to, pyrrolyl, furanyl, thienyl, imidazolyl, oxazolyl, thiazolyl, triazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, pyridinyl, pyrazinyl, pyrazolyl, pyridazinyl, pyrimidinyl, triazinyl, isoxazolyl, benzofuranyl, isothiazolyl, benzothienyl, indolyl, isoindolyl, isobenzofuranyl, benzimidazolyl, benzoxazolyl, benzoisoxazolyl, benzothiazolyl, benzoisothiazolyl, benzooxadiazolyl, benzothiadiazolyl, benzotriazolyl, purinyl, quinolinyl, isoquinolinyl, quinazolinyl or quinoxalinyl. Heteroaryl can be further substituted by halogen, C_{1-6}alkyl, haloC_{1-6}alkyl, cyano, C_{3-7}cycloalkyl, $(C_{1-6}alkyl)_2$amino, C_{1-6}alkoxy. Example of heteroaryl include, but not limited to, chloropyridinyl, chlorothiazolyl, cyanopyrazolyl, cyanopyridinyl, fluorochloropyridinyl, fluoropyrazolyl, fluoropyridinyl, fluoropyrimidinyl, hydroxymethylpyrazolyl, methoxymethylpyrazolyl, methylfluoropyridinyl, methylfluoropyrimidinyl, methylpyrazolyl, trifluoromethylpyridinyl and trifluoromethylthiazolyl.

The term "aryl" denotes a monovalent aromatic carbocyclic mono- or bicyclic ring system comprising 6 to 10 carbon ring atoms. Example of monocyclic aryl include, but not limited to, phenyl; and examples of the bicyclic aryl include, but not limited to, indanyl and bicyclo[4.2.0]octa-1(6),2,4-trienyl.

The term "heterocyclyl" denotes a monovalent saturated or partly unsaturated mono or bicyclic ring system of 3 to 10 ring atoms, comprising 1 to 5 ring heteroatoms selected from N, O and S, the remaining ring atoms being carbon. In particular embodiments, heterocyclyl is a monovalent saturated monocyclic ring system of 4 to 7 ring atoms, comprising 1, 2, or 3 ring heteroatoms selected from N, O and S, the remaining ring atoms being carbon. Examples for monocyclic saturated heterocyclyl are aziridinyl, oxiranyl, azetidinyl, oxetanyl, pyrrolidinyl, tetrahydrofuranyl, tetrahydrothienyl, pyrazolidinyl, imidazolidinyl, oxazolidinyl, isoxazolidinyl, thiazolidinyl, piperidinyl, tetrahydropyranyl, tetrahydrothiopyranyl, piperazinyl, morpholinyl, thiomorpholinyl, 1,1-dioxo-thiomorpholin-4-yl, azepanyl, diazepanyl, homopiperazinyl,

oxazepanyl, and lactam include, but not limited to, oxopyrrolidinyl, oxomorpholinyl, oxooxazolidinyl and oxooxazinanyl; monocyclic saturated heterocyclyl can be further substituted by $(C_{1-6}alkyl)_2$aminocarbonyl, $(C_{1-6}alkyl)_2$morpholinylcarbonyl, C_{1-6}alkoxy, C_{1-6}alkoxyC_{1-6}alkyl, C_{1-6}alkyl, C_{1-6}alkyl, C_{1-6}alkyl(C_{1-6}alkylsulfonyl)amino, C_{1-6}alkylaminocarbonyl, C_{1-6}alkylcarbonylamino, C_{1-6}alkylmorpholinylcarbonyl, C_{1-6}alkyloxadiazolyl, C_{1-6}alkyloxazolyl, C_{1-6}alkylpyrazolyl, C_{1-6}alkylsulfonyl, C_{1-6}alkylsulfonylamino, C_{1-6}alkylsulfonylC_{1-6}alkyl, cyano, dioxopyrrolidinyl, haloC_{1-6}alkyl, haloC_{1-6}alkyloxadiazolyl, halopiperidinylcarbonyl, halopyrimidinylamino, halopyrimidinyloxy, halopyrrolidinylcarbonyl, hydroxy, hydroxyazetidinylcarbonyl, hydroxyC_{1-6}alkyl, hydroxyC_{1-6}alkyl, hydroxyC_{1-6}alkyl(C_{1-6}alkyl)aminocarbonyl, hydroxyC_{1-6}alkylaminocarbonyl, hydroxypyrrolidinylcarbonyl, morpholinylcarbonyl, oxadiazolyl, oxazolyl, oxazolylaminocarbonyl, oxazolyl(C_{1-6}alkyl)aminocarbonyl, oxazolylcarbonyl(C_{1-6}alkyl)amino, oxomorpholinyl, oxooxazolidinyl, oxopyrrolidinyl, phenyl, pyrazolylC_{1-6}alkyl, pyridinyl, pyrimidinyl, pyrimidinylamino, pyrimidinylC_{1-6}alkylamino, pyrimidinyloxy, pyrimidinyloxyC_{1-6}alkyl, pyrrolidinylcarbonyl and thiazolyl. Examples for substituted monocyclic saturated heterocyclyl include, but not limited to difluoropiperidinyl, methyloxooxazinanyl, dimethyloxooxazinanyl, methoxyoxooxazinanyl, morpholinylcarbonyl(methyl)oxooxazinanyl, dimethyloxopyrrolidinyl, oxazolyloxopyrrolidinyl, dimethylmorpholinyl, methyloxomorpholinyl, hydroxypiperidinyl, cyanooxopyrrolidinyl, trifluoromethyloxopyrrolidinyl, hydroxyoxopyrrolidinyl, acetylpiperidinyl, methylaminocarbonyloxopyrrolidinyl, methoxyoxopyrrolidinyl, dimethyloxooxazolidinyl, phenyl(hydroxy)oxopyrrolidinyl, pyrimidinyloxyoxopyrrolidinyl, pyrimidinyloxy(hydroxy)oxopyrrolidinyl, pyrimidinyloxy(hydroxy)(methyl)oxopyrrolidinyl and pyrimidinylaminohydroxyoxopyrrolidinyl. Examples for bicyclic saturated heterocyclic ring are azabicyclo[3.2.1]octyl, quinuclidinyl, oxaazabicyclo[3.2.1]octanyl, azabicyclo[3.3.1]nonanyl, oxaaza-bicyclo[3.3.1]nonanyl, azabicyclo[3.1.0]hexanyl, oxodiazaspiro[3.4]octanyl, acetyloxodiazaspiro[3.4]octanyl, thiaazabicyclo[3.3.1]nonanyl, oxoazaspiro[2.4]heptanyl, oxoazaspiro[3.4]octanyl, oxoazabicyclo[3.1.0]hexanyl and dioxotetrahydropyrrolo[1,2-a]pyrazinyl. Examples for partly unsaturated heterocyclyl include dihydrofuryl, imidazolinyl, dihydrooxazolyl, tetrahydropyridinyl, dioxopiperazinyl, oxoimidazolidinyl, trioxothiazinanyl and dihydropyranyl; partly unsaturated heterocyclyl can be further substituted by halogen, C_{1-6}alkyl, C_{1-6}alkylsulfonyl, examples for substituted partly unsaturated heterocyclyl include, but not limited to, methylimidazolidinyl, methylsulfonyloxoimidazolidinyl and dimethyloxooxazolidinyl.

The term "lactam" denotes a cyclic amide containing from 3 to 10 ring atoms which can comprise one, two or three atoms selected from nitrogen, oxygen and/or sulfur. Lactam can be mono-cyclic ring or bi-cyclic ring which can be further substituted by $(C_{1-6}alkyl)_2$aminocarbonyl, $(C_{1-6}alkyl)_2$morpholinylcarbonyl, C_{1-6}alkoxy, C_{1-6}alkoxyC_{1-6}alkyl, C_{1-6}alkyl, C_{1-6}alkyl, C_{1-6}alkyl(C_{1-6}alkylsulfonyl)amino, C_{1-6}alkylaminocarbonyl, C_{1-6}alkylcarbonylamino, C_{1-6}alkylmorpholinylcarbonyl, C_{1-6}alkyloxadiazolyl, C_{1-6}alkyloxazolyl, C_{1-6}alkylpyrazolyl, C_{1-6}alkylsulfonyl, C_{1-6}alkylsulfonylamino, C_{1-6}alkylsulfonylC_{1-6}alkyl, cyano, dioxopyrrolidinyl, haloC_{1-6}alkyl, haloC_{1-6}alkyloxadiazolyl, halopiperidinylcarbonyl, halopyrimidinylamino, halopyrimidinyloxy, halopyrrolidinylcarbonyl, hydroxy, hydroxyazetidinylcarbonyl, hydroxyC_{1-6}alkyl, hydroxyC_{1-6}alkyl, hydroxyC_{1-6}alkyl(C_{1-6}alkyl)aminocarbonyl, hydroxyC_{1-6}alkylaminocarbonyl, hydroxypyrrolidinylcarbonyl, morpholinylcarbonyl, oxadiazolyl, oxazolyl, oxazolylaminocarbonyl, oxazolyl(C_{1-6}alkyl)aminocarbonyl, oxazolylcarbonyl(C_{1-6}alkyl)amino, oxomorpholinyl, oxooxazolidinyl, oxopyrrolidinyl, phenyl, pyrazolylC_{1-6}alkyl, pyridinyl, pyrimidinyl, pyrimidinylamino, pyrimidinylC_{1-6}alkylamino, pyrimidinyloxy, pyrimidinyloxyC_{1-6}alkyl, pyrrolidinylcarbonyl and thiazolyl . Examples of lactam include, but not limited to, oxooxazinanyl, methyloxooxazinanyl, dimethyloxooxazinanyl, oxopyrrolidinyl, dimethyloxopyrrolidinyl, cyanooxopyrrolidinyl, hydroxyoxopyrrolidinyl, methoxyoxopyrrolidinyl, trifluoromethyloxopyrrolidinyl, oxazolyloxopyrrolidinyl, oxoazabicyclo[3.1.0]hexanyl, oxomorpholinyl, methyloxomorpholinyl, difluoropyrrolidinyloxopyrrolidinyl, dimethyloxooxazolidinyl, phenyl(hydroxy)oxopyrrolidinyl, pyrimidinyloxyoxopyrrolidinyl, pyrimidinyloxy(hydroxy)oxopyrrolidinyl, pyrimidinyloxy(hydroxy)(methyl)oxopyrrolidinyl and pyrimidinylaminohydroxyoxopyrrolidinyl.

The term "diastereomer" denotes a stereoisomer with two or more centers of chirality and whose molecules are not mirror images of one another. Diastereomers have different physical properties, e.g. melting points, boiling points, spectral properties, activities and reactivities.

The term "enantiomers" denotes two stereoisomers of a compound which are non-superimposable mirror images of one another.

The term "pharmaceutically acceptable salts" denotes salts which are not biologically or otherwise undesirable. Pharmaceutically acceptable salts include both acid and base addition salts.

The term "pharmaceutically acceptable acid addition salt" denotes those pharmaceutically acceptable salts formed with inorganic acids such as hydrochloric acid, hydrobromic acid,

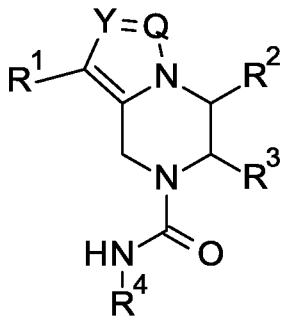
sulfuric acid, nitric acid, carbonic acid, phosphoric acid, and organic acids selected from aliphatic, cycloaliphatic, aromatic, araliphatic, heterocyclic, carboxylic, and sulfonic classes of organic acids such as formic acid, acetic acid, propionic acid, glycolic acid, gluconic acid, lactic acid, pyruvic acid, oxalic acid, malic acid, maleic acid, maloneic acid, succinic acid, fumaric acid, tartaric acid, citric acid, aspartic acid, ascorbic acid, glutamic acid, anthranilic acid, benzoic acid, cinnamic acid, mandelic acid, embonic acid, phenylacetic acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, and salicyclic acid.

The term "pharmaceutically acceptable base addition salt" denotes those pharmaceutically acceptable salts formed with an organic or inorganic base. Examples of acceptable inorganic bases include sodium, potassium, ammonium, calcium, magnesium, iron, zinc, copper, manganese, and aluminum salts. Salts derived from pharmaceutically acceptable organic nontoxic bases includes salts of primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines and basic ion exchange resins, such as isopropylamine, trimethylamine, diethylamine, triethylamine, tripropylamine, ethanolamine, 2-diethylaminoethanol, trimethamine, dicyclohexylamine, lysine, arginine, histidine, caffeine, procaine, hydrabamine, choline, betaine, ethylenediamine, glucosamine, methylglucamine, theobromine, purines, piperizine, piperidine, N-ethylpiperidine, and polyamine resins.

Compounds of the general formula (I) which contain one or several chiral centers can either be present as racemates, diastereomeric mixtures, or optically active single isomers. The racemates can be separated according to known methods into the enantiomers. Particularly, diastereomeric salts which can be separated by crystallization are formed from the racemic mixtures by reaction with an optically active acid such as e.g. D- or L-tartaric acid, mandelic acid, malic acid, lactic acid or camphorsulfonic acid.

INHIBITOR OF HBV

The present invention provides (i) novel compounds having the general formula (I),



(I),

wherein

R^1 is heterocyclyl, said heterocyclyl being unsubstituted or substituted with one, two or three substituents independently selected from $(C_{1-6}alkyl)_2$aminocarbonyl, $(C_{1-6}alkyl)_2$morpholinylcarbonyl, C_{1-6}alkoxy, C_{1-6}alkoxyC_{1-6}alkyl, C_{1-6}alkoxycarbonyl, C_{1-6}alkyl, C_{1-6}alkyl(C_{1-6}alkylsulfonyl)amino, C_{1-6}alkylaminocarbonyl, C_{1-6}alkylcarbonyl, C_{1-6}alkylcarbonylamino, C_{1-6}alkylimidazolyl, C_{1-6}alkylmorpholinylcarbonyl, C_{1-6}alkyloxadiazolyl, C_{1-6}alkyloxazolyl, C_{1-6}alkylpyrazolyl, C_{1-6}alkylsulfonyl, C_{1-6}alkylsulfonylamino, C_{1-6}alkylsulfonylC_{1-6}alkyl, carbamoyl, cyano, dioxopyrrolidinyl, haloC_{1-6}alkyl, haloC_{1-6}alkyloxadiazolyl, halogen, halopiperidinylcarbonyl, halopyridinyl, halopyrimidinylamino, halopyrimidinyloxy, halopyrrolidinylcarbonyl, hydroxy, hydroxyazetidinylcarbonyl, hydroxyC_{1-6}alkyl, hydroxyC_{1-6}alkyl(C_{1-6}alkyl)aminocarbonyl, hydroxyC_{1-6}alkylaminocarbonyl, hydroxypyrrolidinylcarbonyl, morpholinylcarbonyl, oxadiazolyl, oxazolyl, oxazolylaminocarbonyl, oxazolyl(C_{1-6}alkyl)aminocarbonyl, oxazolylcarbonyl, oxazolylcarbonyl(C_{1-6}alkyl)amino, oxomorpholinyl, oxooxazolidinyl, oxopyrrolidinyl, phenyl, phenylcarbonyl, pyrazolylC_{1-6}alkyl, pyridinyl, pyrimidinyl, pyrimidinylamino, pyrimidinyl(C_{1-6}alkyl)amino, pyrimidinyloxy, pyrimidinyloxyC_{1-6}alkyl, pyrrolidinylcarbonyl and thiazolyl;

heteroaryl, said heteroaryl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, C_{1-6}alkyl ,haloC_{1-6}alkyl, hydroxy C_{1-6}alkyl and C_{1-6}alkoxyC_{1-6}alkyl;

phenyl, said phenyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, hydroxy, C_{1-6}alkyl, C_{1-6}alkoxy, C_{3-7}cycloalkyl, haloC_{1-6}alkoxy and haloC_{1-6}alkyl; or

C_{3-7}cycloalkyl;

R^2 and R^3 are independently selected from hydrogen and C_{1-6}alkyl;

R^4 is heteroaryl, said heteroaryl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, C_{1-6}alkyl, haloC_{1-6}alkyl, C_{1-6}alkoxy, C_{3-7}cycloalkyl and $(C_{1-6}alkyl)_2$amino;

aryl, said aryl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, C_{3-7}cycloalkyl, C_{1-6}alkyl, C_{2-6}alkynyl, C_{1-6}alkoxy, haloC_{1-6}alkyl and haloC_{1-6}alkoxy;

phenylC_{1-6}alkyl, said phenylC_{1-6}alkyl being unsubstituted or substituted with one, two or three halogen; or

C_{3-7}cycloalkyl;

Y and Q are independently selected from CH and N;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of the present invention is (ii) a compound of formula (I), wherein

R^1 is azabicyclo[3.1.0]hexanyl;

dioxopiperazinyl;

dioxopyrimidinyl;

dioxotetrahydropyrrolo[1,2-a]pyrazinyl;

morpholinyl, said morpholinyl being unsubstituted or substituted with one, two or three C_{1-6}alkyl;

oxaazabicyclo[3.2.1]octanyl;

oxoazabicyclo[3.1.0]hexanyl;

oxoazaspiro[2.4]heptanyl, said oxoazaspiro[2.4]heptanyl being unsubstituted or substituted with hydroxy;

oxoazaspiro[4.4]nonanyl;

oxoazaspiro[3.4]octanyl, said oxoazaspiro[3.4]octanyl being unsubstituted or substituted with hydroxy;

oxodiazaspiro[3.4]octanyl, said oxodiazaspiro[3.4]octanyl being unsubstituted or substituted with one, two or three substituents independently selected from C_{1-6}alkylcarbonyl, C_{1-6}alkoxycarbonyl, oxazolylcarbonyl and pyrimidinyl;

oxodihydropyrazolo[1,5-a]pyrazinyl;

oxohexahydropyrimidinyl;

oxoimidazolidinyl, said oxoimidazolidinyl being unsubstituted or substituted with one, two or three substituents independently selected from C_{1-6}alkyl, C_{1-6}alkylcarbonyl, C_{1-6}alkylsulfonyl, phenyl, phenylcarbonyl and pyrimidinyl;

oxoindolinyl;

oxoisoindolinyl;

oxomorpholinyl, said oxomorpholinyl being unsubstituted or substituted with one, two or three substituents independently selected from C_{1-6}alkyl and oxazolyl;

oxooxaazaspiro[2.4]heptanyl;

oxooxaazaspiro[3.4]octanyl;

oxooxaazaspiro[4.4]nonanyl;

oxooxaazaspiro[4.5]decanyl;

oxooxazinanyl, said oxooxazinanyl being unsubstituted or substituted with one, two or three substituents independently selected from C_{1-6}alkyl, C_{1-6}alkoxy and morpholinylcarbonyl;

oxooxazolidinyl, said oxooxazolidinyl being unsubstituted or substituted with one, two or three substituents independently selected from C_{1-6}alkyl, phenyl, pyridinyl, halopyridinyl, oxazolyl, C_{1-6}alkylimidazolyl and C_{1-6}alkyloxadiazolyl;

oxopiperidyl, said oxopiperidyl being unsubstituted or substituted with one, two or three substituents independently selected from C_{1-6}alkyl and hydroxy;

oxopyrrolidinyl, said oxopyrrolidinyl being unsubstituted or substituted with one, two or three substituents independently selected from $(C_{1-6}alkyl)_2$aminocarbonyl, $(C_{1-6}alkyl)_2$morpholinylcarbonyl, C_{1-6}alkoxy, C_{1-6}alkoxyC_{1-6}alkyl, C_{1-6}alkyl, C_{1-6}alkyl(C_{1-6}alkylsulfonyl)amino, C_{1-6}alkylaminocarbonyl, C_{1-6}alkylcarbonylamino, C_{1-6}alkylmorpholinylcarbonyl, C_{1-6}alkyloxadiazolyl, C_{1-6}alkyloxazolyl, C_{1-6}alkylpyrazolyl, C_{1-6}alkylsulfonyl, C_{1-6}alkylsulfonylamino, C_{1-6}alkylsulfonylC_{1-6}alkyl, cyano, dioxopyrrolidinyl, haloC_{1-6}alkyl, haloC_{1-6}alkyloxadiazolyl, halopiperidinylcarbonyl, halopyrimidinylamino, halopyrimidinyloxy, halopyrrolidinylcarbonyl, hydroxy, hydroxyazetidinylcarbonyl, hydroxyC_{1-6}alkyl, hydroxyC_{1-6}alkyl(C_{1-6}alkyl)aminocarbonyl, hydroxyC_{1-6}alkylaminocarbonyl, hydroxypyrrolidinylcarbonyl, morpholinylcarbonyl, oxadiazolyl, oxazolyl, oxazolylaminocarbonyl, oxazolyl(C_{1-6}alkyl)aminocarbonyl,

oxazolylcarbonyl(C_{1-6}alkyl)amino, oxomorpholinyl, oxooxazolidinyl, oxopyrrolidinyl, phenyl, pyrazolylC_{1-6}alkyl, pyridinyl, pyrimidinyl, pyrimidinylamino, pyrimidinylC_{1-6}alkylamino, pyrimidinyloxy, pyrimidinyloxyC_{1-6}alkyl, pyrrolidinylcarbonyl and thiazolyl;

oxopyrrolo[3,2-c]pyridinyl;

oxopyrrolo[3,4-b]pyridinyl;

oxotetrahydrofuro[3,4-c]pyrrolyl;

oxotetrahydroimidazo[5,1-c][1,4]oxazinyl;

piperidinyl, said piperidinyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, hydroxy and C_{1-6}alkylcarbonyl;

pyrazolyl, said pyrazolyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, C_{1-6}alkyl, hydroxyC_{1-6}alkyl and C_{1-6}alkoxyC_{1-6}alkyl;

pyridinyl, said pyridinyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, C_{1-6}alkyl and haloC_{1-6}alkyl;

pyrimidinyl, said pyrimidinyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen and C_{1-6}alkyl;

pyrrolidinyl, said pyrrolidinyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, hydroxy, C_{1-6}alkyl, haloC_{1-6}alkyl, C_{1-6}alkoxy and C_{1-6}alkoxyC_{1-6}alkyl;

tetrahydrofuranyl;

thiazolyl, said thiazolyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen and haloC_{1-6}alkyl;

phenyl, said phenyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, hydroxy, C_{3-7}cycloalkyl, C_{1-6}alkyl, C_{1-6}alkoxy, haloC_{1-6}alkyl and haloC_{1-6}alkoxy;or

C_{3-7}cycloalkyl;

R^2 and R^3 are independently selected from hydrogen and C_{1-6}alkyl;

R^4 is benzofuranyl;

benzothiophenyl;

benzoxazolyl;

indolyl;

C_{1-6}alkylbenzothiazolyl;

pyridinyl, said pyridinyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, C_{1-6}alkyl, C_{3-7}cycloalkyl, C_{1-6}alkoxy, haloC_{1-6}alkyl and (C_{1-6}alkyl)$_2$amino;

bicyclo[4.2.0]octa-1(6),2,4-trienyl;

indanyl;

phenyl, said phenyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, C_{3-7}cycloalkyl, C_{1-6}alkyl, C_{2-6}alkynyl, C_{1-6}alkoxy, haloC_{1-6}alkyl and haloC_{1-6}alkoxy;

phenylC_{1-6}alkyl, said phenylC_{1-6}alkyl being unsubstituted or substituted with one, two or three halogen;

or C_{3-7}cycloalkyl;

Y and Q are independently selected from CH and N;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of the present invention is (iii) a compound of formula (I), wherein

R^1 is pyrazolyl substituted by halogen, cyano, C_{1-6}alkyl, hydroxyC_{1-6}alkyl or C_{1-6}alkoxyC_{1-6}alkyl;

pyridinyl, said pyridinyl being unsubstituted or substituted with one or two substituents independently selected from halogen, cyano, C_{1-6}alkyl and haloC_{1-6}alkyl;

pyrimidinyl substituted with one or two substituents independently selected from halogen and C_{1-6}alkyl;

thiazolyl, said thiazolyl being unsubstituted or substituted by halogen or haloC_{1-6}alkyl;

phenyl, said phenyl being unsubstituted or substituted with one or two substituents independently selected from halogen, cyano, hydroxy, C_{3-7}cycloalkyl, C_{1-6}alkyl, C_{1-6}alkoxy, haloC_{1-6}alkyl and haloC_{1-6}alkoxy;

R^2 and R^3 are independently selected from hydrogen and C_{1-6}alkyl with the proviso that R^2 and R^3 are not C_{1-6}alkyl simultaneously;

R^4 is benzothiophenyl;

benzoxazolyl;

indolyl;

benzothiazolyl substituted by C_{1-6}alkyl;

pyridinyl, said pyridinyl being unsubstituted or substituted with one or two substituents independently selected from halogen, cyano, C_{1-6}alkyl, C_{3-7}cycloalkyl, C_{1-6}alkoxy, haloC_{1-6}alkyl and $(C_{1-6}alkyl)_2$amino;

bicyclo[4.2.0]octa-1(6),2,4-trienyl;

phenyl, said phenyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, C_{3-7}cycloalkyl, C_{1-6}alkyl, C_{2-6}alkynyl, C_{1-6}alkoxy, haloC_{1-6}alkyl and haloC_{1-6}alkoxy;

phenylC_{1-6}alkyl, said phenylC_{1-6}alkyl being unsubstituted or substituted with one or two halogen;

or C_{3-7}cycloalkyl;

Y and Q are independently selected from CH and N;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of the present invention is (iv) a compound of formula (I), wherein

R^1 is fluorophenyl, phenyl, chlorophenyl, trifluoromethylphenyl, cyanophenyl, methoxyphenyl, methylphenyl, difluorophenyl, fluorochlorophenyl, difluoromethylphenyl, methylfluorophenyl, cyclopropylphenyl, hydroxyphenyl, trifluoromethoxyphenyl, bromophenyl, methylpyrazolyl, cyanopyrazolyl, fluoropyrazolyl, hydroxymethylpyrazolyl, methoxymethylpyrazolyl, trifluoromethylpyridinyl, cyanopyridinyl, methylfluoropyridinyl, pyridinyl, chloropyridinyl, fluoropyridinyl, fluorochloropyridinyl, fluoropyrimidinyl, methylfluoropyrimidinyl, thiazolyl, trifluoromethylthiazolyl or chlorothiazolyl;

R^2 and R^3 are independently selected from hydrogen and methyl with the proviso that R^2 and R^3 are not methyl simultaneously;

R^4 is phenyl, trifluoromethylphenyl, fluorochlorophenyl, fluorophenyl, chlorophenyl, cyanophenyl, pyridinyl, methylfluoropyridinyl, fluorotrifluoromethylphenyl, trifluorophenyl, fluorochlorobenzyl, dichlorobenzyl, methylchloropyridinyl, methylbenzothiazolyl, benzothiophenyl, trifluoromethylpyridinyl, difluorophenyl, fluorocyanophenyl, indolyl, methylfluorophenyl, chloropyridinyl, cyanopyridinyl, chloromethoxypyridinyl, methyltrifluoromethylphenyl, chlorotrifluoromethylphenyl, chlorocyanophenyl, ethylphenyl, ethynylphenyl, isopropylphenyl, methoxyphenyl,

ethynylfluorophenyl, dimethylpyridinyl, fluorobromophenyl, difluoromethoxyphenyl, fluorotrifluoromethoxyphenyl, difluoromethylphenyl, methylphenyl, difluorocyanophenyl, fluorochloropyridinyl, cyclopropylphenyl, methyldifluorophenyl, difluorochlorophenyl, cyclopropyldifluorophenyl, difluoroethylphenyl, cyclopropylfluorophenyl, methoxydifluorophenyl, benzyl, fluoropyridinyl, benzoxazolyl, methylpyridinyl, difluoropyridinyl, cyclopentyl, cyclohexyl, bicyclo[4.2.0]octa-1(6),2,4-trienyl, bromopyridinyl, cyclopropylpyridinyl, dimethylaminopyridinyl or difluoromethylpyridinyl;

Y and Q are independently selected from CH and N;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of the present invention is (v) a compound of formula (I), wherein R^1 is phenyl, said phenyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, hydroxy, C_{3-7}cycloalkyl, C_{1-6}alkyl, C_{1-6}alkoxy, haloC_{1-6}alkyl and haloC_{1-6}alkoxy; or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of the present invention is (vi) a compound of formula (I), wherein R^1 is phenyl, bromophenyl, chlorophenyl, cyanophenyl, cyclopropylphenyl, difluorophenyl, difluoromethylphenyl, fluorophenyl, fluorochlorophenyl, fluoromethylphenyl, hydroxyphenyl, methoxyphenyl, methylphenyl, trifluoromethoxyphenyl or trifluoromethylphenyl; or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of the present invention is (vii) a compound of formula (I), wherein R^4 is phenyl, said phenyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, C_{3-7}cycloalkyl, C_{1-6}alkyl, C_{2-6}alkynyl, C_{1-6}alkoxy, haloC_{1-6}alkyl and haloC_{1-6}alkoxy; or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of the present invention is (viii) a compound of formula (I), wherein R^4 is phenyl, chlorophenyl, chlorocyanophenyl, chlorotrifluoromethylphenyl, cyanophenyl, cyclopropylphenyl, difluorophenyl, difluoroethylphenyl, difluoromethoxyphenyl, difluoromethylphenyl, ethylphenyl, ethynylphenyl, fluorophenyl, fluorobromophenyl,

fluorochlorophenyl, fluorocyanophenyl, fluorocyclopropylphenyl, fluoroethynylphenyl, difluorochlorophenyl, difluorocyanophenyl, difluorocyclopropylphenyl, methoxydifluorophenyl, methyldifluorophenyl, methylfluorophenyl, fluorotrifluoromethoxyphenyl, fluorotrifluoromethylphenyl, isopropylphenyl, methoxyphenyl, methylphenyl, methyltrifluoromethylphenyl, trifluorophenyl or trifluoromethylphenyl; or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of the present invention is (ix) a compound of formula (I), wherein

R^1 is pyrazolyl substituted by halogen or hydroxyC_{1-6}alkyl;

pyridinyl substituted by halogen;

pyrimidinyl substituted by halogen;

phenyl substituted once or twice by halogen;

R^2 is H;

R^3 is H or C_{1-6}alkyl;

R^4 is pyridinyl substituted by haloC_{1-6}alkyl; or

phenyl substituted with one, two or three substituents independently selected from halogen and cyano;

Y and Q are independently selected from CH and N, with proviso that Y and Q are not CH simultaneously;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of the present invention is (x) a compound of formula (I), wherein

R^1 is fluoropyrazolyl, hydroxymethylpyroazolyl, fluoropyridinyl, fluoropyrimidinyl, fluorophenyl or difluorophenyl;

R^2 is H;

R^3 is H or methyl;

R^4 is difluoromethylpyridinyl, fluorochlorophenyl, fluorocyanophenyl or trifluorophenyl;

Y and Q are independently selected from CH and N, with proviso that Y and Q are not CH simultaneously;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

In another embodiment of the present invention, particular compounds of the present invention are (xi) selected from:

N-(3-cyano-4-fluoro-phenyl)-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(5-fluoro-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(5-fluoro-2-pyridyl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-fluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-1-(2,4-difluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

1-(2,4-difluorophenyl)-N-(3,4,5-trifluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(2,4-difluorophenyl)-6,7-dihydro-4H-triazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(4-fluoropyrazol-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-[2-(difluoromethyl)-4-pyridyl]-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(5-fluoropyrimidin-2-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide; and

(6S)-3-[4-(hydroxymethyl)pyrazol-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

Another embodiment of present invention is (xii) a compound of formula (I), wherein

R^1 is azabicyclo[3.1.0]hexanyl;

morpholinyl, said morpholinyl being unsubstituted or substituted twice by C_{1-6}alkyl;

oxaazabicyclo[3.2.1]octanyl;

piperidinyl, said piperidinyl being unsubstituted or substituted with one or two substituents independently selected from halogen, hydroxy and C_{1-6}alkylcarbonyl;

pyrrolidinyl, said pyrrolidinyl being unsubstituted or substituted with one or two substituents independently selected from halogen, cyano, hydroxy, C_{1-6}alkyl, haloC_{1-6}alkyl, C_{1-6}alkoxy and C_{1-6}alkoxyC_{1-6}alkyl;

tetrahydrofuranyl; or

C_{3-7}cycloalkyl;

R^2 is H;

R^3 is H or C_{1-6}alkyl;

R^4 is benzofuranyl;

pyridinyl, said pyridinyl being substituted with one or two substituents independently selected from halogen and haloC_{1-6}alkyl;

indanyl;

phenyl, said phenyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano and C_{1-6}alkyl; or

phenylC_{1-6}alkyl;

Y is CH when Q is N; or Y is N when Q is CH;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of present invention is (xiii) a compound of formula (I), wherein

R^1 is azabicyclo[3.1.0]hexanyl, cyclohexyl, cyclopentyl, morpholinyl, dimethylmorpholinyl, oxaazabicyclo[3.2.1]octanyl, piperidinyl, difluoropiperidinyl, hydroxypiperidinyl, acetylpiperidinyl, pyrrolidinyl, methylpyrrolidinyl, methoxymethylpyrrolidinyl, methoxypyrrolidinyl, trifluoromethylpyrrolidinyl, cyanopyrrolidinyl, methylhydroxypyrrolidinyl, difluoropyrrolidinyl or tetrahydrofuranyl;

R^2 is H;

R^3 is H or methyl;

R^4 is benzofuranyl, indanyl, benzyl, phenyl, fluorochlorophenyl, fluorocyanophenyl, trifluorophenyl, methyldifluorophenyl, chloropyridinyl, fluorochloropyridinyl or trifluoromethylpyridinyl;

Y is CH when Q is N; or Y is N when Q is CH;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

Another embodiment of present invention is (xiv) a compound of formula (I), wherein

R^1 is dioxopiperazinyl;

dioxopyrimidinyl

dioxotetrahydropyrrolo[1,2-a]pyrazinyl;

oxoazabicyclo[3.1.0]hexanyl;

oxoazaspiro[2.4]heptanyl, said oxoazaspiro[2.4]heptanyl being unsubstituted or substituted with hydroxy;

oxoazaspiro[4.4]nonanyl;

oxoazaspiro[3.4]octanyl, said oxoazaspiro[3.4]octanyl being unsubstituted or substituted with hydroxy;

oxodiazaspiro[3.4]octanyl, said oxodiazaspiro[3.4]octanyl being substituted by C_{1-6}alkylcarbonyl, C_{1-6}alkoxycarbonyl, oxazolylcarbonyl or pyrimidinyl;

oxodihydropyrazolo[1,5-a]pyrazinyl;

oxohexahydropyrimidinyl;

oxoimidazolidinyl, said oxoimidazolidinyl being unsubstituted or substituted with one or two substituents independently selected from C_{1-6}alkyl, C_{1-6}alkylcarbonyl, C_{1-6}alkylsulfonyl, phenyl, phenylcarbonyl and pyrimidinyl;

oxoindolinyl;

oxomorpholinyl, said oxomorpholinyl being unsubstituted or substituted with one or two substituents independently selected from C_{1-6}alkyl and oxazolyl;

oxooxaazaspiro[2.4]heptanyl;

oxooxaazaspiro[3.4]octanyl;

oxooxaazaspiro[4.4]nonanyl;

oxooxaazaspiro[4.5]decanyl;

oxooxazinanyl, said oxooxazinanyl being unsubstituted or substituted with one or two substituents independently selected from C_{1-6}alkyl, C_{1-6}alkoxy and morpholinylcarbonyl;

oxooxazolidinyl, said oxooxazolidinyl being unsubstituted or substituted with one or two substituents independently selected from C_{1-6}alkyl, phenyl, pyridinyl, halopyridinyl, oxazolyl, C_{1-6}alkylimidazolyl and C_{1-6}alkyloxadiazolyl;

oxopiperidyl substituted by C_{1-6}alkyl or hydroxy;

oxopyrrolidinyl, said oxopyrrolidinyl being unsubstituted or substituted with one, two or three substituents independently selected from $(C_{1-6}alkyl)_2$aminocarbonyl, $(C_{1-6}alkyl)_2$morpholinylcarbonyl, C_{1-6}alkoxy, C_{1-}

$_{6}$alkoxyC_{1-6}alkyl, C_{1-6}alkyl, C_{1-6}alkyl(C_{1-6}alkylsulfonyl)amino, C_{1-6}alkylaminocarbonyl, C_{1-6}alkylcarbonylamino, C_{1-6}alkylmorpholinylcarbonyl, C_{1-6}alkyloxadiazolyl, C_{1-6}alkyloxazolyl, C_{1-6}alkylpyrazolyl, C_{1-6}alkylsulfonyl, C_{1-6}alkylsulfonylamino, C_{1-6}alkylsulfonylC_{1-6}alkyl, cyano, dioxopyrrolidinyl, haloC_{1-6}alkyl, haloC_{1-6}alkyloxadiazolyl, halopiperidinylcarbonyl, halopyrimidinylamino, halopyrimidinyloxy, halopyrrolidinylcarbonyl, hydroxy, hydroxyazetidinylcarbonyl, hydroxyC_{1-6}alkyl, hydroxyC_{1-6}alkyl, hydroxyC_{1-6}alkyl(C_{1-6}alkyl)aminocarbonyl, hydroxyC_{1-6}alkylaminocarbonyl, hydroxypyrrolidinylcarbonyl, morpholinylcarbonyl, oxadiazolyl, oxazolyl, oxazolylaminocarbonyl, oxazolyl(C_{1-6}alkyl)aminocarbonyl, oxazolylcarbonyl(C_{1-6}alkyl)amino, oxomorpholinyl, oxooxazolidinyl, oxopyrrolidinyl, phenyl, pyrazolylC_{1-6}alkyl, pyridinyl, pyrimidinyl, pyrimidinylamino, pyrimidinyl(C_{1-6}alkyl)amino, pyrimidinyloxy, pyrimidinyloxyC_{1-6}alkyl, pyrrolidinylcarbonyl and thiazolyl;

oxopyrrolo[3,2-c]pyridinyl;

oxopyrrolo[3,4-b]pyridinyl;

oxotetrahydrofuro[3,4-c]pyrrolyl;

oxotetrahydroimidazo[5,1-c][1,4]oxazinyl;

R^2 and R^3 are independently selected from hydrogen and C_{1-6}alkyl with the proviso that R^2 is not C_{1-6}alkyl when R^3 is H;

R^4 is pyridinyl substituted with one or two substituents independently selected from halogen and haloC_{1-6}alkyl;

phenyl substituted with one, two or three substituents independently selected from halogen and haloC_{1-6}alkyl;

Y is CH;

Q is N;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of present invention is (xv) a compound of formula (I), wherein

R^1 is dioxopiperazinyl, dioxopyrimidinyl, dioxotetrahydropyrrolo[1,2-a]pyrazinyl, oxoazabicyclo[3.1.0]hexanyl, oxoazaspiro[2.4]heptanyl, hydroxy oxoazaspiro[2.4]heptanyl, oxoazaspiro[4.4]nonanyl, oxoazaspiro[3.4]octanyl, hydroxyoxoazaspiro[3.4]octanyl, acetyloxodiazaspiro[3.4]octanyl,

methoxycarbonyloxodiazaspiro[3.4]octanyl,
ethoxycarbonyloxodiazaspiro[3.4]octanyl,
oxazolylcarbonyloxodiazaspiro[3.4]octanyl, pyrimidinyloxodiazaspiro[3.4]octanyl,
oxodihydropyrazolo[1,5-a]pyrazinyl, oxohexahydropyrimidinyl, oxoimidazolidinyl,
acetyloxoimidazolidinyl, benzoyloxoimidazolidinyl, dimethyloxoimidazolidinyl,
methyloxoimidazolidinyl, methylsulfonyloxoimidazolidinyl,
phenyloxoimidazolidinyl, pyrimidinyloxoimidazolidinyl, oxoindolinyl,
oxoisoindolinyl, oxomorpholinyl, methyloxomorpholinyl, dimethyloxomorpholinyl,
oxazolyloxomorpholinyl, oxooxaazaspiro[4.5]decanyl, oxooxaazaspiro[4.4]nonanyl,
oxooxaazaspiro[2.4]heptanyl, oxooxaazaspiro[3.4]octanyl, oxooxazinanyl,
methyloxooxazinanyl, dimethyloxooxazinanyl, methoxyoxooxazinanyl,
morpholinylcarbonyl(methyl)oxooxazinanyl, oxooxazolidinyl,
dimethyloxooxazolidinyl, chloropyridinyloxooxazolidinyl,
fluoropyridinyloxooxazolidinyl, methyloxooxazolidinyl,
methylimidazolyloxooxazolidinyl, methyloxadiazolyloxooxazolidinyl,
oxazolyloxooxazolidinyl, phenyloxooxazolidinyl, pyridinyloxooxazolidinyl,
hydroxyoxopiperidyl, methyloxopiperidyl, oxopyrrolidinyl,
acetylaminooxopyrrolidinyl, cyanooxopyrrolidinyl,
difluoropiperidinylcarbonyl(methyl)oxopyrrolidinyl,
difluoropyrrolidinylcarbonyloxopyrrolidinyl,
difluoropyrrolidinylcarbonyl(methyl)oxopyrrolidinyl, dihydroxyoxopyrrolidinyl,
dimethyloxopyrrolidinyl, dimethylaminocarbonyloxopyrrolidinyl,
dimethylmorpholinylcarbonyloxopyrrolidinyl, dioxopyrrolidinyloxopyrrolidinyl,
ethyloxopyrrolidinyl, fluoropyrimidinylaminooxopyrrolidinyl,
fluoropyrimidinyloxyoxopyrrolidinyl, hydroxyoxopyrrolidinyl,
hydroxyazetidinylcarbonyloxopyrrolidinyl,
hydroxyethyl(methyl)aminocarbonyloxopyrrolidinyl,
hydroxy(dimethyl)oxopyrrolidinyl, hydroxydimethylethylaminooxopyrrolidinyl,
hydroxymethyloxopyrrolidinyl, hydroxy(methyl)cyanooxopyrrolidinyl,
hydroxymethyl(cyano)oxopyrrolidinyl, hydroxymethylethyloxopyrrolidinyl,
hydroxypyrrolidinylcarbonyloxopyrrolidinyl, methoxyoxopyrrolidinyl,
methoxymethyloxopyrrolidinyl, methyloxopyrrolidinyl,
methyl(methylsulfonyl)aminooxopyrrolidinyl, methylaminocarbonyloxopyrrolidinyl,

methylcyanooxopyrrolidinyl, methyl(hydroxymethyl)oxopyrrolidinyl, methylmorpholinylcarbonyloxopyrrolidinyl, methyloxadiazolyloxopyrrolidinyl, methyloxadiazolyl(methyl)oxopyrrolidinyl, methyloxazolyloxopyrrolidinyl, methylpyrazolyloxopyrrolidinyl, methylsulfonyloxopyrrolidinyl, methylsulfonylaminooxopyrrolidinyl, methylsulfonylmethyloxopyrrolidinyl, morpholinylcarbonyloxopyrrolidinyl, morpholinylcarbonyl(methyl)oxopyrrolidinyl, oxadiazolyloxopyrrolidinyl, oxadiazolyl(methyl)oxopyrrolidinyl, oxazolyloxopyrrolidinyl, oxazolylaminocarbonyloxopyrrolidinyl, oxazolylcarbonyl(methyl)aminooxopyrrolidinyl, oxazolyl(methyl)aminocarbonyloxopyrrolidinyl, oxomorpholinyloxopyrrolidinyl, oxooxazolidinyloxopyrrolidinyl, oxopyrrolidinyloxopyrrolidinyl, phenyloxopyrrolidinyl, phenyl(hydroxy)oxopyrrolidinyl, pyrazolylmethyloxopyrrolidinyl, pyridinyloxopyrrolidinyl, pyrimidinyloxopyrrolidinyl, pyrimidinylaminooxopyrrolidinyl, pyrimidinyl(methyl)aminooxopyrrolidinyl, pyrimidinyloxyoxopyrrolidinyl, pyrimidinyloxy(hydroxy)oxopyrrolidinyl, pyrimidinyloxy(hydroxy)(methyl)oxopyrrolidinyl, pyrimidinyloxymethyloxopyrrolidinyl, pyrrolidinylcarbonyloxopyrrolidinyl, thiazolyloxopyrrolidinyl, trifluoromethyloxopyrrolidinyl, trifluoromethyloxadiazolyloxopyrrolidinyl, oxotetrahydrofuro[3,4-c]pyrrolyl, oxotetrahydroimidazo[5,1-c][1,4]oxazinyl, oxopyrrolo[3,4-b]pyridinyl or oxopyrrolo[3,2-c]pyridinyl;

R^2 and R^3 are independently selected from hydrogen and methyl with the proviso that R^2 is not methyl when R^3 is H;

R^4 is chloropyridinyl, difluoromethylpyridinyl, fluorochloropyridinyl, fluorodifluoromethylpyridinyl, trifluoromethylpyridinyl, difluorochlorophenyl, difluorodifluoromethylphenyl, fluorochlorophenyl, fluorotrifluoromethylphenyl, trifluorophenyl;

Y is CH;

Q is N;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of present invention is (xvi) a compound of formula (I), wherein R^1 is

oxoazabicyclo[3.1.0]hexanyl;

oxodiazaspiro[3.4]octanyl substituted by C_{1-6}alkoxycarbonyl or pyrimidinyl;

oxoimidazolidinyl;

oxoindolinyl;

oxomorpholinyl, said oxomorpholinyl being unsubstituted or substituted once or twice by C_{1-6}alkyl;

oxooxaazaspiro[2.4]heptanyl;

oxooxaazaspiro[4.5]decanyl;

oxooxazinanyl, said oxooxazinanyl being unsubstituted or substituted once or twice by C_{1-6}alkyl;

oxooxazolidinyl, said oxooxazolidinyl being unsubstituted or substituted twice by C_{1-6}alkyl;

oxopyrrolidinyl said oxopyrrolidinyl being unsubstituted or substituted with one or two substituents independently selected from $(C_{1-6}alkyl)_2$aminocarbonyl, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkyloxadiazolyl, cyano, halopyrimidinyloxy, haloC_{1-6}alkyl, hydroxy, hydroxyC_{1-6}alkyl, morpholinylcarbonyl, oxadiazolyl, pyrimidinylamino, pyrimidinyloxy and pyrrolidinylcarbonyl;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of present invention is (xvii) a compound of formula (I), wherein R^1 is oxoazabicyclo[3.1.0]hexanyl, methoxycarbonyloxodiazaspiro[3.4]octanyl, ethoxycarbonyloxodiazaspiro[3.4]octanyl, pyrimidinyloxodiazaspiro[3.4]octanyl, oxoimidazolidinyl, oxoindolinyl, oxomorpholinyl, dimethyloxomorpholinyl, oxooxaazaspiro[4.5]decanyl, oxooxaazaspiro[2.4]heptanyl, oxooxazinanyl, methyloxooxazinanyl, dimethyloxooxazinanyl, oxooxazolidinyl, dimethyloxooxazolidinyl, oxopyrrolidinyl, cyanooxopyrrolidinyl, hydroxyoxopyrrolidinyl, methoxyoxopyrrolidinyl, trifluoromethyloxopyrrolidinyl, pyrimidinylaminooxopyrrolidinyl, oxadiazolyloxopyrrolidinyl, methyloxadiazolyloxopyrrolidinyl, hydroxymethylcyanooxopyrrolidinyl, methylcyanooxopyrrolidinyl, methyl(hydroxymethyl)oxopyrrolidinyl, morpholinylcarbonyloxopyrrolidinyl, pyrimidinyloxyoxopyrrolidinyl, pyrimidinyloxy(hydroxy)oxopyrrolidinyl, fluoropyrimidinyloxyoxopyrrolidinyl,

dimethylaminocarbonyloxopyrrolidinyl or pyrrolidinylcarbonyloxopyrrolidinyl; or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of present invention is (xviii) a compound of formula (I), wherein R^4 is pyridinyl substituted by haloC_{1-6}alkyl; or phenyl substituted with two or three substituents independently selected from halogen and haloC_{1-6}alkyl; or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of present invention is (xix) a compound of formula (I), wherein R^4 is difluoromethylpyridinyl, fluorochlorophenyl, difluorodifluoromethylphenyl or trifluorophenyl; or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of present invention is (xx) a compound of formula (I), wherein

R^1 is oxoazabicyclo[3.1.0]hexanyl;

oxodiazaspiro[3.4]octanyl substituted with C_{1-6}alkoxycarbonyl or pyrimidinyl;

oxoimidazolidinyl;

oxoindolinyl;

oxomorpholinyl, said oxomorpholinyl being unsubstituted or substituted once or twice by C_{1-6}alkyl;

oxooxaazaspiro[2.4]heptanyl;

oxooxaazaspiro[4.5]decanyl;

oxooxazinanyl, said oxooxazinanyl being unsubstituted or substituted once ro twice by C_{1-6}alkyl;

oxooxazolidinyl, said oxooxazolidinyl being unsubstituted or substituted once or twice by C_{1-6}alkyl;

oxopyrrolidinyl said oxopyrrolidinyl being unsubstituted or substituted with one or two substituents independently selected from $(C_{1-6}alkyl)_2$aminocarbonyl, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkyloxadiazolyl, cyano, halopyrimidinyloxy, haloC_{1-6}alkyl, hydroxy, hydroxyC_{1-6}alkyl, morpholinylcarbonyl, oxadiazolyl, pyrimidinylamino, pyrimidinyloxy and pyrrolidinylcarbonyl;

R^2 is H;

R^3 is H or C_{1-6}alkyl;

R^4 is pyridinyl substituted by haloC_{1-6}alkyl; or

phenyl substituted with two or three substituents independently selected from halogen and haloC_{1-6}alkyl;

Y is CH;

Q is N;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of present invention is (xxi) a compound of formula (I), wherein

R^1 is oxoazabicyclo[3.1.0]hexanyl, methoxycarbonyloxodiazaspiro[3.4]octanyl, ethoxycarbonyloxodiazaspiro[3.4]octanyl, pyrimidinyloxodiazaspiro[3.4]octanyl, oxoimidazolidinyl, oxoindolinyl, oxomorpholinyl, dimethyloxomorpholinyl, oxooxaazaspiro[4.5]decanyl, oxooxaazaspiro[2.4]heptanyl, oxooxazinanyl, methyloxooxazinanyl, dimethyloxooxazinanyl, oxooxazolidinyl, dimethyloxooxazolidinyl, oxopyrrolidinyl, cyanooxopyrrolidinyl, hydroxyoxopyrrolidinyl, methoxyoxopyrrolidinyl, trifluoromethyloxopyrrolidinyl, pyrimidinylaminooxopyrrolidinyl, oxadiazolyloxopyrrolidinyl, methyloxadiazolyloxopyrrolidinyl, hydroxymethylcyanooxopyrrolidinyl, methylcyanooxopyrrolidinyl, methyl(hydroxymethyl)oxopyrrolidinyl, morpholinylcarbonyloxopyrrolidinyl, pyrimidinyloxyoxopyrrolidinyl, pyrimidinyloxy(hydroxy)oxopyrrolidinyl, fluoropyrimidinyloxyoxopyrrolidinyl, dimethylaminocarbonyloxopyrrolidinyl or pyrrolidinylcarbonyloxopyrrolidinyl;

R^2 is H;

R^3 is H or methyl;

R^4 is difluoromethylpyridinyl, fluorochlorophenyl, difluorodifluoromethylphenyl or trifluorophenyl;

Y is CH;

Q is N;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

In another embodiment of the present invention, particular compounds of the present invention are (xxii) selected from:

N-(3-chloro-4-fluoro-phenyl)-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

6-methyl-3-(2-oxopyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-cyano-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-hydroxy-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(3-oxomorpholin-4-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(2-oxooxazolidin-3-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-methoxy-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(4-cyano-2-oxo-pyrrolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4R)-4-cyano-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4S)-4-cyano-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-6-methyl-3-[2-oxo-4-(trifluoromethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(5,5-dimethyl-2-oxo-oxazolidin-3-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxo-3-azabicyclo[3.1.0]hexan-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(pyrimidin-2-ylamino)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-6-methyl-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-3-(5,5-dimethyl-2-oxo-oxazolidin-3-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-3-(5,5-dimethyl-2-oxo-oxazolidin-3-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(5-methyl-2-oxo-1,3-oxazinan-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(1,3,4-oxadiazol-2-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(5-methyl-1,3,4-oxadiazol-2-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(3-methyl-1,2,4-oxadiazol-5-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(5-methyl-1,2,4-oxadiazol-3-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxo-1,3-oxazinan-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(5,5-dimethyl-2-oxo-1,3-oxazinan-3-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(3-oxo-8-oxa-2-azaspiro[4.5]decan-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(5-oxo-4-oxa-6-azaspiro[2.4]heptan-6-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

methyl 6-[(6S)-6-methyl-5-[(3,4,5-trifluorophenyl)carbamoyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-7-oxo-2,6-diazaspiro[3.4]octane-2-carboxylate;

ethyl 6-[(6S)-6-methyl-5-[(3,4,5-trifluorophenyl)carbamoyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-7-oxo-2,6-diazaspiro[3.4]octane-2-carboxylate;

(6S)-6-methyl-3-(7-oxo-2-pyrimidin-2-yl-2,6-diazaspiro[3.4]octan-6-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxoindolin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxopyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-cyano-4-(hydroxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(4-cyano-4-methyl-2-oxo-pyrrolidin-1-yl)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(hydroxymethyl)-4-methyl-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(2,2-dimethyl-5-oxo-morpholin-4-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-6-methyl-3-(2-oxoimidazolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4S)-4-methoxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4R)-4-methoxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[(4S)-2-oxo-4-pyrimidin-2-yloxy-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4S)-4-(5-fluoropyrimidin-2-yl)oxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(dimethylcarbamoyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(pyrrolidine-1-carbonyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[(4R)-2-oxo-4-pyrimidin-2-yloxy-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(3-cyano-2-methyl-5-oxo-pyrrolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(5-hydroxy-2-oxo-1,3-oxazinan-3-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide; and

(6S)-3-[(3S,4R)-3-hydroxy-2-oxo-4-pyrimidin-2-yloxy-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

Another embodiment of present invention is (xxiii) a compound of formula (I), wherein

R^1 is oxopyrrolidinyl, said oxopyrrolidinyl being unsubstituted or substituted with one or two substituents independently selected from $(C_{1-6}alkyl)_2$aminocarbonyl, $(C_{1-6}alkyl)_2$morpholinylcarbonyl, C_{1-6}alkoxy, C_{1-6}alkoxyC_{1-6}alkyl, C_{1-6}alkyl, C_{1-6}alkyl(C_{1-6}alkylsulfonyl)amino, C_{1-6}alkylaminocarbonyl, C_{1-6}alkylcarbonylamino, C_{1-6}alkylmorpholinylcarbonyl, C_{1-6}alkyloxadiazolyl, C_{1-6}alkyloxazolyl, C_{1-6}alkylpyrazolyl, C_{1-6}alkylsulfonyl, C_{1-6}alkylsulfonylamino, C_{1-6}alkylsulfonylC_{1-6}alkyl, cyano, dioxopyrrolidinyl, haloC_{1-6}alkyl, haloC_{1-6}alkyloxadiazolyl, halopiperidinylcarbonyl, halopyrimidinylamino, halopyrimidinyloxy, halopyrrolidinylcarbonyl, hydroxy, hydroxyazetidinylcarbonyl, hydroxyC_{1-6}alkyl, hydroxyC_{1-6}alkyl(C_{1-6}alkyl)aminocarbonyl, hydroxyC_{1-6}alkylaminocarbonyl, hydroxypyrrolidinylcarbonyl, morpholinylcarbonyl, oxadiazolyl, oxazolyl, oxazolylaminocarbonyl, oxazolyl(C_{1-6}alkyl)aminocarbonyl, oxazolylcarbonyl(C_{1-6}alkyl)amino, oxomorpholinyl, oxooxazolidinyl, oxopyrrolidinyl, phenyl, pyrazolylC_{1-6}alkyl, pyridinyl, pyrimidinyl, pyrimidinylamino, pyrimidinyl(C_{1-6}alkyl)amino, pyrimidinyloxy, pyrimidinyloxyC_{1-6}alkyl, pyrrolidinylcarbonyl and thiazolyl;

R^2 and R^3 are independently selected from hydrogen and C_{1-6}alkyl with the proviso that R^2 is not C_{1-6}alkyl when R^3 is H;

R^4 is pyridinyl substituted with one or two substituents independently selected from halogen and haloC_{1-6}alkyl;

phenyl substituted with one, two or three substituents independently selected from halogen and haloC_{1-6}alkyl;

Y is CH;

Q is N;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of present invention is (xxiv) a compound of formula (I), wherein R^1 is oxopyrrolidinyl, acetylaminooxopyrrolidinyl, cyanooxopyrrolidinyl, difluoropiperidinylcarbonyl(methyl)oxopyrrolidinyl, difluoropyrrolidinylcarbonyloxopyrrolidinyl, difluoropyrrolidinylcarbonyl(methyl)oxopyrrolidinyl, dihydroxyoxopyrrolidinyl, dimethyloxopyrrolidinyl, dimethylaminocarbonyloxopyrrolidinyl, dimethylmorpholinylcarbonyloxopyrrolidinyl, dioxopyrrolidinyloxopyrrolidinyl, ethyloxopyrrolidinyl, fluoropyrimidinylaminooxopyrrolidinyl, fluoropyrimidinyloxyoxopyrrolidinyl, hydroxyoxopyrrolidinyl, hydroxyazetidinylcarbonyloxopyrrolidinyl, hydroxyethyl(methyl)aminocarbonyloxopyrrolidinyl, hydroxy(dimethyl)oxopyrrolidinyl, hydroxydimethylethylaminooxopyrrolidinyl, hydroxymethyloxopyrrolidinyl, hydroxy(methyl)cyanooxopyrrolidinyl, hydroxymethyl(cyano)oxopyrrolidinyl, hydroxymethylethyloxopyrrolidinyl, hydroxypyrrolidinylcarbonyloxopyrrolidinyl, methoxyoxopyrrolidinyl, methoxymethyloxopyrrolidinyl, methyloxopyrrolidinyl, methyl(methylsulfonyl)aminooxopyrrolidinyl, methylaminocarbonyloxopyrrolidinyl, methylcyanooxopyrrolidinyl, methyl(hydroxymethyl)oxopyrrolidinyl, methylmorpholinylcarbonyloxopyrrolidinyl, methyloxadiazolyloxopyrrolidinyl, methyloxadiazolyl(methyl)oxopyrrolidinyl, methyloxazolyloxopyrrolidinyl, methylpyrazolyloxopyrrolidinyl, methylsulfonyloxopyrrolidinyl, methylsulfonylaminooxopyrrolidinyl, methylsulfonylmethyloxopyrrolidinyl, morpholinylcarbonyloxopyrrolidinyl, morpholinylcarbonyl(methyl)oxopyrrolidinyl, oxadiazolyloxopyrrolidinyl, oxadiazolyl(methyl)oxopyrrolidinyl, oxazolyloxopyrrolidinyl, oxazolylaminocarbonyloxopyrrolidinyl, oxazolylcarbonyl(methyl)aminooxopyrrolidinyl, oxazolyl(methyl)aminocarbonyloxopyrrolidinyl, oxomorpholinyloxopyrrolidinyl, oxooxazolidinyloxopyrrolidinyl, oxopyrrolidinyloxopyrrolidinyl, phenyloxopyrrolidinyl, phenyl(hydroxy)oxopyrrolidinyl, pyrazolylmethyloxopyrrolidinyl, pyridinyloxopyrrolidinyl, pyrimidinyloxopyrrolidinyl, pyrimidinylaminooxopyrrolidinyl, pyrimidinyl(methyl)aminooxopyrrolidinyl, pyrimidinyloxyoxopyrrolidinyl,

pyrimidinyloxy(hydroxy)oxopyrrolidinyl,
pyrimidinyloxy(hydroxy)(methyl)oxopyrrolidinyl,
pyrimidinyloxymethyloxopyrrolidinyl, pyrrolidinylcarbonyloxopyrrolidinyl,
thiazolyloxopyrrolidinyl, trifluoromethyloxopyrrolidinyl or
trifluoromethyloxadiazolyloxopyrrolidinyl;

R^2 and R^3 are independently selected from hydrogen and methyl with the proviso that R^2 is not methyl when R^3 is H;

R^4 is chloropyridinyl, difluoromethylpyridinyl, fluorochloropyridinyl, trifluoromethylpyridinyl, difluorochlorophenyl, difluorodifluoromethylphenyl, fluorochlorophenyl, fluorotrifluoromethylphenyl or trifluorophenyl;

Y is CH;

Q is N;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of present invention is (xxv) a compound of formula (I), wherein R^1 is oxopyrrolidinyl, said oxopyrrolidinyl being unsubstituted or substituted with one or two substituents independently selected from $(C_{1-6}alkyl)_2$aminocarbonyl, C_{1-6}alkoxy, C_{1-6}alkyl, C_{1-6}alkyloxadiazolyl, cyano, haloC_{1-6}alkyl, halopyrimidinyloxy, hydroxy, hydroxyC_{1-6}alkyl, morpholinylcarbonyl, oxadiazolyl, pyrimidinylamino, pyrimidinyloxy and pyrrolidinylcarbonyl; or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of present invention is (xxvi) a compound of formula (I), wherein R^1 is oxopyrrolidinyl, cyanooxopyrrolidinyl, hydroxyoxopyrrolidinyl, methoxyoxopyrrolidinyl, trifluoromethyloxopyrrolidinyl, pyrimidinylaminooxopyrrolidinyl, oxadiazolyloxopyrrolidinyl, methyloxadiazolyloxopyrrolidinyl, hydroxymethylcyanooxopyrrolidinyl, methylcyanooxopyrrolidinyl, methyl(hydroxymethyl)oxopyrrolidinyl, pyrimidinyloxyoxopyrrolidinyl, pyrimidinyloxy(hydroxy)oxopyrrolidinyl, fluoropyrimidinyloxyoxopyrrolidinyl, morpholinylcarbonyloxopyrrolidinyl, dimethylaminocarbonyloxopyrrolidinyl or pyrrolidinylcarbonyloxopyrrolidinyl; or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of present invention is (xxvii) a compound of formula (I), wherein R^2 is H; R^3 is H or C_{1-6}alkyl; or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of present invention is (xxviii) a compound of formula (I), wherein R^2 is H; R^3 is H or methyl; or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of present invention is (xxix) a compound of formula (I), wherein R^4 is pyridinyl substituted by haloC_{1-6}alkyl; or phenyl substituted with one, two or three substituents independently selected from halogen and haloC_{1-6}alkyl; or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of present invention is (xxx) a compound of formula (I), wherein R^4 is difluoromethylpyridinyl, fluorochlorophenyl, difluorodifluoromethylphenyl or trifluorophenyl; or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of present invention is (xxxi) a compound of formula (I), wherein

R^1 is oxopyrrolidinyl, said oxopyrrolidinyl being unsubstituted or substituted with one or two substituents independently selected from $(C_{1-6}alkyl)_2$aminocarbonyl, C_{1-6}alkoxy, C_{1-6}alkyl, C_{1-6}alkyloxadiazolyl, cyano, haloC_{1-6}alkyl, halopyrimidinyloxy, hydroxy, hydroxyC_{1-6}alkyl, morpholinylcarbonyl, oxadiazolyl, pyrimidinylamino, pyrimidinyloxy and pyrrolidinylcarbonyl;

R^2 is H;

R^3 is H or C_{1-6}alkyl;

R^4 is pyridinyl substituted by haloC_{1-6}alkyl; or

phenyl substituted with one, two or three substituents independently selected from halogen and haloC_{1-6}alkyl;

Y is CH;

Q is N;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of present invention is (xxxii) a compound of formula (I), wherein

R^1 is oxopyrrolidinyl, cyanooxopyrrolidinyl, hydroxyoxopyrrolidinyl, methoxyoxopyrrolidinyl, trifluoromethyloxopyrrolidinyl, pyrimidinylaminooxopyrrolidinyl, oxadiazolyloxopyrrolidinyl, methyloxadiazolyloxopyrrolidinyl, hydroxymethylcyanooxopyrrolidinyl, methylcyanooxopyrrolidinyl, methyl(hydroxymethyl)oxopyrrolidinyl, pyrimidinyloxyoxopyrrolidinyl, pyrimidinyloxy(hydroxy)oxopyrrolidinyl, fluoropyrimidinyloxyoxopyrrolidinyl, morpholinylcarbonyloxopyrrolidinyl, dimethylaminocarbonyloxopyrrolidinyl or pyrrolidinylcarbonyloxopyrrolidinyl;

R^2 is H;

R^3 is H or $C_{1\text{-}6}$alkyl;

R^4 is difluoromethylpyridinyl, fluorochlorophenyl, difluorodifluoromethylphenyl or trifluorophenyl;

Y is CH;

Q is N;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

In another embodiment of the present invention, particular compounds of the present invention are (xxxiii) selected from:

N-(3-chloro-4-fluoro-phenyl)-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

6-methyl-3-(2-oxopyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-cyano-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-hydroxy-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-methoxy-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(4-cyano-2-oxo-pyrrolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4R)-4-cyano-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4S)-4-cyano-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-6-methyl-3-[2-oxo-4-(trifluoromethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(pyrimidin-2-ylamino)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(1,3,4-oxadiazol-2-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(5-methyl-1,3,4-oxadiazol-2-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(3-methyl-1,2,4-oxadiazol-5-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(5-methyl-1,2,4-oxadiazol-3-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxopyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-cyano-4-(hydroxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(4-cyano-4-methyl-2-oxo-pyrrolidin-1-yl)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(hydroxymethyl)-4-methyl-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4S)-4-methoxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4R)-4-methoxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[(4S)-2-oxo-4-pyrimidin-2-yloxy-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4S)-4-(5-fluoropyrimidin-2-yl)oxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(morpholine-4-carbonyl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(dimethylcarbamoyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(pyrrolidine-1-carbonyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

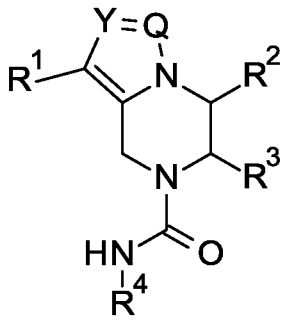
(6S)-6-methyl-3-[(4R)-2-oxo-4-pyrimidin-2-yloxy-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(3-cyano-2-methyl-5-oxo-pyrrolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide; and

(6S)-3-[(3S,4R)-3-hydroxy-2-oxo-4-pyrimidin-2-yloxy-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

The present invention provides (xxxiv) novel compounds having the general formula (I),



(I),

wherein

R^1 is heterocyclyl, said heterocyclyl being unsubstituted or substituted with one to three substituents independently selected from C_{1-6}alkyl, haloC_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkoxyC_{1-6}alkyl, C_{1-6}alkylcarbonyl, C_{1-6}alkylaminocarbonyl, C_{1-6}alkylsulfonyl, halogen, cyano, hydroxy, oxadiazolyl and oxazolyl;

heteroaryl, said heteroaryl being unsubstituted or substituted with one to three substituents independently selected from halogen, cyano, C_{1-6}alkyl and haloC_{1-6}alkyl;

phenyl, said phenyl being unsubstituted or substituted with one to three substituents independently selected from halogen, cyano, hydroxy, C_{1-6}alkyl, C_{1-6}alkoxy, C_{3-7}cycloalkyl, haloC_{1-6}alkoxy and haloC_{1-6}alkyl; or

C_{3-7}cycloalkyl;

R^2 and R^3 are independently selected from hydrogen and C_{1-6}alkyl;

R^4 is heterocyclyl, said heterocyclyl being unsubstituted or substituted with one to three substituents independently selected from halogen and C_{1-6}alkyl;

heteroaryl, said heteroaryl being unsubstituted or substituted with one to three substituents independently selected from halogen, cyano, C_{1-6}alkyl, haloC_{1-6}alkyl, C_{1-6}alkoxy, C_{3-7}cycloalkyl and $(C_{1-6}alkyl)_2$amino;

aryl, said aryl being unsubstituted or substituted with one to three substituents independently selected from halogen, cyano, C_{3-7}cycloalkyl, C_{1-6}alkyl, C_{2-6}alkynyl, C_{1-6}alkoxy, haloC_{1-6}alkyl and haloC_{1-6}alkoxy;

phenylC_{1-6}alkyl, said phenylC_{1-6}alkyl being unsubstituted or substituted with halogen; or

C_{3-7}cycloalkyl;

Y and Q are independently selected from CH and N;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of the present invention is (xxxv) a compound of formula (I), wherein R^1 is

heterocyclyl, said heterocyclyl being unsubstituted or substituted with one to three substituents independently selected from C_{1-6}alkyl, C_{1-6}alkoxy, haloC_{1-6}alkyl, cyano, hydroxy, C_{1-6}alkylsulfonyl and oxazolyl;

heteroaryl, said heteroaryl being unsubstituted or substituted with one to three substituents independently selected from halogen, cyano, haloC_{1-6}alkyl and C_{1-6}alkyl;

phenyl, said phenyl being unsubstituted or substituted with one to three halogen; or

C_{3-7}cycloalkyl;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of the present invention is (xxxvi) a compound of formula (I), wherein R^1 is

oxopyrrolidinyl, dimethyloxopyrrolidinyl, cyanooxopyrrolidinyl, hydroxyoxopyrrolidinyl, methoxyoxopyrrolidinyl, trifluoromethyloxopyrrolidinyl, oxazolyloxopyrrolidinyl, azabicyclo[3.1.0]hexanyl, oxoazabicyclo[3.1.0]hexanyl, oxomorpholinyl, methyloxomorpholinyl, oxooxazolidinyl, dimethyloxooxazolidinyl, dimethyloxoimidazolidinyl, methylsulfonyloxoimidazolidinyl, trioxothiazinanyl, fluoropyrimidinyl, trifluoromethylpyridinyl, methylfluoropyridinyl, fluoropyridinyl, methylpyrazolyl, cyanopyrazolyl, fluoropyrazolyl, fluorophenyl, difluorophenyl, cyclopentyl or cyclohexyl;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of the present invention is (xxxvii) a compound of formula (I), wherein R^4 is

phenyl, said phenyl being unsubstituted or substituted with one to three substituents independently selected from halogen, cyano, C_{3-7}cycloalkyl, C_{1-6}alkyl, haloC_{1-6}alkyl and C_{2-6}alkynyl; or

pyridinyl, said pyridinyl being unsubstituted or substituted with one to three substituents independently selected from halogen, C_{1-6}alkyl and haloC_{1-6}alkyl;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

A further embodiment of the present invention is (xxxviii) a compound of formula (I), wherein R^4 is fluorophenyl, chlorophenyl, fluorochlorophenyl, fluorotrifluoromethylphenyl, trifluorophenyl, fluorocyanophenyl, methylfluorophenyl, ethynylfluorophenyl, cyclopropylfluorophenyl, methyldifluorophenyl, difluorochlorophenyl, difluoromethyldifluorophenyl, fluoropyridinyl, chloropyridinyl, methylpyridinyl or difluoromethylpyridinyl;or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

Another embodiment of the present invention is (xxxix) a compound of formula (I), wherein Y and Q are independently selected from CH and N, provided that Y and Q are not CH simultaneously;or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

Another embodiment of the present invention is (xl) a compound of formula (I), wherein R^1 is oxopyrrolidinyl, oxomorpholinyl or oxooxazolidinyl, said oxopyrrolidinyl, oxomorpholinyl and oxooxazolidinyl being unsubstituted or substituted with

one to three substituents independently selected from C_{1-6}alkyl, haloC_{1-6}alkyl, C_{1-6}alkoxy, cyano, oxazolyl and hydroxy;

pyridinyl, pyrimidinyl or pyrazolyl, said pyridinyl, pyrimidinyl or pyrazolyl being unsubstituted or substituted with one to three substituents independently selected from halogen and cyano;

phenyl, said phenyl being unsubstituted or substituted with halogen; or

C_{3-7}cycloalkyl;

R^2 and R^3 are independently selected from hydrogen and C_{1-6}alkyl;

R^4 is phenyl or pyridinyl, said phenyl or pyridinyl being unsubstituted or substituted with one to three substituents independently selected from halogen, cyano and haloC_{1-6}alkyl; or

C_{3-7}cycloalkyl;

Y and Q are independently selected from CH and N, provided that Y and Q are not CH simultaneously;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

Another embodiment of the present invention is (xli) a compound of formula (I), wherein

R^1 is oxopyrrolidinyl, cyanooxopyrrolidinyl, hydroxyoxopyrrolidinyl, methoxyoxopyrrolidinyl, trifluoromethyloxopyrrolidinyl, oxomorpholinyl, methyloxomorpholinyl, oxazolyloxopyrrolidinyl, oxooxazolidinyl, fluoropyrimidinyl, fluoropyridinyl, cyanopyrazolyl, fluoropyrazolyl, fluorophenyl, difluorophenyl or cyclopentyl;

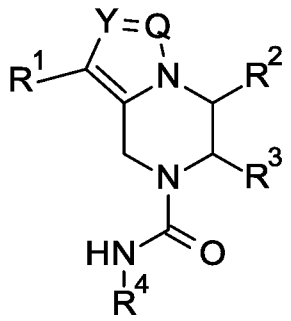
R^2 and R^3 are independently selected from hydrogen and methyl;

R^4 is fluorochlorophenyl, fluorocyanophenyl, trifluorophenyl, difluoromethyldifluorophenyl, difluoromethylpyridinyl;

Y and Q are independently selected from CH and N, provided that Y and Q are not CH simultaneously;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

In another embodiment, the present invention provides novel compounds having the general formula (I),



(I),

wherein

R^1 is heterocyclyl, said heterocyclyl being unsubstituted or substituted with cyano;

heteroaryl, said heteroaryl being unsubstituted or substituted independently with one, two or three halogen;

phenyl, said phenyl being unsubstituted or substituted independently with one, two or three halogen; or

lactam, said lactam being unsubstituted or substituted with cyano;

R^2 and R^3 are independently selected from hydrogen and C_{1-6}alkyl;

R^4 is phenyl, said phenyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen and cyano; or

pyridinyl, said pyridinyl being unsubstituted or substituted with haloC_{1-6}alkyl;

Y and Q are independently selected from C and N;

or pharmaceutically acceptable salts, enantiomers or diastereomers thereof.

Another embodiment of present invention is a compound of formula (I),

wherein

R^1 is fluorophenyl, difluorophenyl, fluoropyrimidinyl, morpholinyl, oxopyrrolidinyl, cyanooxopyrrolidinyl or oxomorpholinyl;

R^2 and R^3 are independently selected from hydrogen and methyl;

R^4 is fluorochlorophenyl, cyanofluorophenyl, trifluorophenyl or difluoromethylpyridinyl;

Y and Q are independently selected from C and N;

or pharmaceutically acceptable salts, enantiomers or diastereomers thereof.

A further embodiment of present invention is a compound of formula (I), wherein R^1 is phenyl, said phenyl being unsubstituted or substituted independently with one, two or three halogen;

pyrimidinyl, said pyrimidinyl being unsubstituted or substituted independently with one, two or three halogen;

morpholinyl;

or lactam, said lactam being unsubstituted or substituted with cyano;

or pharmaceutically acceptable salts, enantiomers or diastereomers thereof.

In another embodiment of the present invention, compounds of the present invention are selected from:

3-(4-fluorophenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N,3-diphenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(3-fluorophenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(3-chlorophenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-phenyl-3-[3-(trifluoromethyl)phenyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2-fluorophenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2-chlorophenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-phenyl-3-[2-(trifluoromethyl)phenyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

1-(4-fluorophenyl)-N-phenyl-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

3-(4-fluorophenyl)-N-phenyl-6,7-dihydro-4H-triazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluorophenyl)-N-[3-(trifluoromethyl)phenyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-8-(4-fluorophenyl)-3,4-dihydro-1H-pyrrolo[1,2-a]pyrazine-2-carboxamide;

N-(2-fluorophenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N,3-bis(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chlorophenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyanophenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(4-chlorophenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2-cyanophenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
N-(3-fluorophenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
N-(4-chloro-3-fluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
N-(3-chloro-4-fluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
3-(4-fluorophenyl)-N-(4-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
N-(4-cyanophenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
N-(3-chloro-4-fluoro-phenyl)-3-(2-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
3-(3-methoxyphenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
3-cyclopentyl-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
3-(2-methoxyphenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
N-phenyl-3-[4-(trifluoromethyl)-2-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
3-(4-cyano-2-pyridyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
N-(3-chlorophenyl)-3-(2-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
N-(3-chlorophenyl)-3-(o-tolyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
N-(5-fluoro-6-methyl-2-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
3-(2-fluorophenyl)-N-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
3-(2-fluorophenyl)-N-[4-fluoro-3-(trifluoromethyl)phenyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
N-(3-chlorophenyl)-3-(2,4-difluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
N-(3-chlorophenyl)-3-(2,3-difluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
3-(3-cyano-2-pyridyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(3-chloro-2-fluoro-phenyl)-N-(3-chlorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(5-chloro-2-fluoro-phenyl)-N-(3-chlorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chlorophenyl)-3-(2,5-difluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-[3-(difluoromethyl)phenyl]-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(5-fluoro-6-methyl-2-pyridyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(5-fluoro-4-methyl-2-pyridyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-phenyl-3-(2-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide+H31;

N-phenyl-3-thiazol-2-yl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-phenyl-3-[4-(trifluoromethyl)thiazol-2-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(5-chlorothiazol-2-yl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(3,4-difluorophenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(6-chloro-2-pyridyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(2,4-difluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2,4-difluorophenyl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluoro-3-methyl-phenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluorophenyl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-[(3-chloro-4-fluoro-phenyl)methyl]-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-[(3,5-dichlorophenyl)methyl]-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(4-chloro-5-methyl-2-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-chloro-2-pyridyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-[(2-chloro-3-fluoro-phenyl)methyl]-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-[(2,6-dichlorophenyl)methyl]-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2,4-difluorophenyl)-N-(5-fluoro-6-methyl-2-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(4-fluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluorophenyl)-N-(2-methyl-1,3-benzothiazol-5-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(benzothiophen-3-yl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2,4-difluorophenyl)-N-[2-(trifluoromethyl)-4-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(3-cyclopropylphenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2-hydroxyphenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-[4-(trifluoromethyl)-2-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(5-fluoro-4-methyl-2-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(5-fluoro-2-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2-chloro-4-pyridyl)-3-(2,4-difluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-[4-(trifluoromethyl)-2-pyridyl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N,3-bis(3-chloro-4-fluoro-phenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-cyclohexyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyano-4-fluoro-phenyl)-3-(5-fluoro-4-methyl-2-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(5-fluoro-2-pyridyl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyano-4-fluoro-phenyl)-3-(5-fluoro-2-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluorophenyl)-N-(1H-indol-6-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-cyclopentyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyano-4-fluoro-phenyl)-3-cyclopentyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluorophenyl)-N-[4-fluoro-3-(trifluoromethyl)phenyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(4-fluoro-3-methyl-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-cyclopentyl-N-indan-5-yl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-cyclopentyl-N-indan-1-yl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-benzyl-3-cyclopentyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyano-4-fluoro-phenyl)-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyano-4-fluoro-phenyl)-3-(4-fluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-pyrrolidin-1-yl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2,4-difluorophenyl)-6-methyl-N-[2-(trifluoromethyl)-4-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(1-piperidyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(4,4-difluoro-1-piperidyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-thiazol-2-yl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2-chloro-4-pyridyl)-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(5-fluoro-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(3,3-difluoro-1-piperidyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2-chloro-4-pyridyl)-3-cyclopentyl-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2-cyano-4-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2-chloro-6-methoxy-4-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(5-fluoro-2-pyridyl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyano-4-fluoro-phenyl)-3-(5-fluoro-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6R)-N-(3-chloro-4-fluoro-phenyl)-3-(4-fluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-fluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2-chloro-4-pyridyl)-3-cyclopentyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(benzofuran-6-yl)-3-cyclopentyl-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyano-4-fluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyano-5-fluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluorophenyl)-N-[4-methyl-3-(trifluoromethyl)phenyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-[3-chloro-5-(trifluoromethyl)phenyl]-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3,4-difluorophenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-cyano-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluorophenyl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3,5-difluorophenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-[4-chloro-3-(trifluoromethyl)phenyl]-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-ethylphenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-ethynylphenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluorophenyl)-N-(3-isopropylphenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluorophenyl)-N-(3-methoxyphenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-phenyl-3-[2-(trifluoromethoxy)phenyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(3-chloro-4-fluoro-phenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(m-tolyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(3-bromophenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-ethynyl-4-fluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-5-fluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2-chloro-4-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2,6-dimethyl-4-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluorophenyl)-N-[2-(trifluoromethyl)-4-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-1-(4-fluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

N-(3-bromo-4-fluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-[3-(difluoromethoxy)phenyl]-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluorophenyl)-N-[4-fluoro-3-(trifluoromethoxy)phenyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-[3-(difluoromethyl)phenyl]-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluorophenyl)-N-(m-tolyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-phenyl-3-[3-(trifluoromethoxy)phenyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

1-(2,4-difluorophenyl)-N-(3-ethynyl-4-fluoro-phenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-1-(2,4-difluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

N-(3-cyano-4-fluoro-phenyl)-1-(2,4-difluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

N-(3-cyano-4,5-difluoro-phenyl)-1-(2,4-difluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

1-(2,4-difluorophenyl)-N-(3,4,5-trifluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

3-(2,4-difluorophenyl)-N-(3-ethynyl-4-fluoro-phenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(6-chloro-5-fluoro-2-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyclopropylphenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyano-4-fluoro-phenyl)-3-(2,4-difluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(6-chloro-5-fluoro-2-pyridyl)-3-(2,4-difluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3,4-difluoro-5-methyl-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4,5-difluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyclopropyl-4,5-difluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-[3-(1,1-difluoroethyl)phenyl]-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(4-chloro-5-fluoro-2-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(2-chloro-5-fluoro-4-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyclopropyl-4-fluoro-phenyl)-3-(2,4-difluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2-chloro-4-pyridyl)-1-(2,4-difluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

1-(2,4-difluorophenyl)-N-[2-(trifluoromethyl)-4-pyridyl]-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-triazolo[1,5-a]pyrazine-5-carboxamide;

N-(6-chloro-5-fluoro-2-pyridyl)-1-(2,4-difluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(2,4-difluorophenyl)-6,7-dihydro-4H-triazolo[1,5-a]pyrazine-5-carboxamide;

N-(3,4-difluoro-5-methyl-phenyl)-3-(5-fluoro-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyclopropyl-4-fluoro-phenyl)-3-(5-fluoro-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4,5-difluoro-phenyl)-3-(5-fluoro-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3,4-difluoro-5-methoxy-phenyl)-3-(5-fluoro-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyclopropyl-4,5-difluoro-phenyl)-3-(5-fluoro-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(6-chloro-5-fluoro-2-pyridyl)-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-1-cyclopentyl-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

1-cyclopentyl-N-(3,4,5-trifluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

1-cyclopentyl-N-(3,4-difluoro-5-methyl-phenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

N-(3-cyclopropyl-4,5-difluoro-phenyl)-1-(2,4-difluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

N-(3,4-difluoro-5-methoxy-phenyl)-1-(2,4-difluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

N-(3,4-difluoro-5-methyl-phenyl)-1-(2,4-difluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(2-methylpyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-morpholino-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(4-methylpyrazol-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-benzyl-3-(4-fluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluorophenyl)-N-(2-fluoro-4-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2,4-difluorophenyl)-N-(2-fluoro-4-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(1,3-benzoxazol-6-yl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluorophenyl)-N-(2-methyl-4-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2,6-difluoro-4-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2,4-difluorophenyl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2,4-difluorophenyl)-N-(5-fluoro-4-methyl-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-cyclopentyl-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-cyclohexyl-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-tetrahydrofuran-3-yl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

6-methyl-3-(2-oxopyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(4-bicyclo[4.2.0]octa-1(6),2,4-trienyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(5-fluoropyrimidin-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(5-fluoro-4-methyl-pyrimidin-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2,4-difluorophenyl)-6-methyl-N-(2-methyl-4-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2-chloro-4-pyridyl)-3-(5-fluoro-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(4-methylpyrazol-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2-chloro-4-pyridyl)-6-methyl-3-[4-(trifluoromethyl)-2-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2-chloro-4-pyridyl)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2-bromo-4-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-2-methyl-4-pyridyl)-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2,4-difluorophenyl)-N-(5-fluoro-2-methyl-4-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(5-chloro-2-methyl-4-pyridyl)-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-[(2-chloro-3-fluoro-phenyl)methyl]-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2,4-difluorophenyl)-N-(5-fluoro-6-methyl-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(5-fluoro-2-pyridyl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(4-methylpyrazol-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(4-cyanopyrazol-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(4-fluoropyrazol-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-[4-fluoro-3-(trifluoromethyl)phenyl]-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-cyclopentyl-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-cyclopentyl-6-methyl-N-[2-(trifluoromethyl)-4-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(6-chloro-5-fluoro-2-pyridyl)-3-cyclopentyl-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2-cyclopropyl-4-pyridyl)-3-(2,4-difluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2,4-difluorophenyl)-N-[2-(dimethylamino)-4-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-[2-(methoxymethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-[3-(methoxymethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(3-methoxypyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(4,4-dimethyl-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-[3-(trifluoromethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(3-cyanopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(3-azabicyclo[3.1.0]hexan-3-yl)-N-(3-chloro-4-fluoro-phenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(3-hydroxy-3-methyl-pyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(2,2-dimethylmorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-[2-(difluoromethyl)-4-pyridyl]-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(3-methyl-5-oxo-morpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(3,3-difluoropyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-[trans-2,6-dimethylmorpholin-4-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-[cis-2,6-dimethylmorpholin-4-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-hydroxy-1-piperidyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(3-methyl-2-oxo-imidazolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-cyano-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(4-fluorophenyl)-7-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4,5-difluoro-phenyl)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-hydroxy-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(3-oxomorpholin-4-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(1-acetyl-4-piperidyl)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4,5-difluoro-phenyl)-6-methyl-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-[4-(methylcarbamoyl)-2-oxo-pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(2-oxooxazolidin-3-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-methoxy-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(4-cyano-2-oxo-pyrrolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4R)-4-cyano-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4S)-4-cyano-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-6-methyl-3-[2-oxo-4-(trifluoromethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(2-acetyl-7-oxo-2,6-diazaspiro[3.4]octan-6-yl)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-methyl-5-oxo-morpholin-4-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(2,5-dioxopiperazin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4,4-dimethyl-2-oxo-imidazolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(3,6-dioxo-4,7,8,8a-tetrahydro-1H-pyrrolo[1,2-a]pyrazin-2-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(4-oxazol-5-yl-2-oxo-pyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(3-methylsulfonyl-5-oxo-imidazolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(5,5-dimethyl-2-oxo-oxazolidin-3-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S,7S)-6,7-dimethyl-3-(2-oxopyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(6-oxo-5-azaspiro[2.4]heptan-5-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxo-3-azabicyclo[3.1.0]hexan-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(4-methyl-2-oxo-pyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-[2-oxo-4-(trifluoromethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(3-hydroxy-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4,4-dimethyl-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-3-(4,4-dimethyl-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(trifluoromethyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(2-chloro-4-pyridyl)-6-methyl-3-[2-oxo-4-(trifluoromethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S,7R)-6,7-dimethyl-3-(2-oxopyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(3S)-3-hydroxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(6-chloro-5-fluoro-2-pyridyl)-3-(4,4-dimethyl-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(3R)-3-hydroxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[6-(difluoromethyl)-5-fluoro-2-pyridyl]-6-methyl-3-(3-oxo-2-azaspiro[4.4]nonan-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-6-methyl-3-(3-oxo-2-azaspiro[4.4]nonan-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(pyrimidin-2-yloxymethyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(pyrazol-1-ylmethyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(pyrimidin-2-ylamino)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-[(5-fluoropyrimidin-4-yl)amino]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-6-methyl-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-3-(5,5-dimethyl-2-oxo-oxazolidin-3-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S,7S)-6,7-dimethyl-3-(2-oxoimidazolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S,7S)-6,7-dimethyl-3-(3-oxomorpholin-4-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(3-benzoyl-5-oxo-imidazolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-3-(5,5-dimethyl-2-oxo-oxazolidin-3-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[6-(difluoromethyl)-5-fluoro-2-pyridyl]-3-(5,5-dimethyl-2-oxo-oxazolidin-3-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(5-methyl-2-oxo-1,3-oxazinan-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(2,4-dioxo-1H-pyrimidin-3-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(2,4-dioxopyrimidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(5-oxo-3-pyrimidin-2-yl-imidazolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(1,3,4-oxadiazol-2-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(5-methyl-1,3,4-oxadiazol-2-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(3-methyl-1,2,4-oxadiazol-5-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(5-methyl-1,2,4-oxadiazol-3-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-[5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl]pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-3-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[5-(1-methylimidazol-2-yl)-2-oxo-oxazolidin-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxo-4-thiazol-5-yl-pyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxo-4-thiazol-2-yl-pyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxo-1,3-oxazinan-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxohexahydropyrimidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(5,5-dimethyl-2-oxo-1,3-oxazinan-3-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-[4-(methoxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(3-oxo-8-oxa-2-azaspiro[4.5]decan-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(3-methyl-2-oxo-pyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-[4-(hydroxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(methoxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(methoxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-[2-(trifluoromethyl)-4-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(4-oxo-3,3a,6,6a-tetrahydro-1H-furo[3,4-c]pyrrol-5-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-ethyl-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(8-oxo-2-oxa-7-azaspiro[4.4]nonan-7-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(4-methylsulfonyl-2-oxo-pyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-hydroxy-2-oxo-1-piperidyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(methylsulfonylmethyl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-[[methyl(methylsulfonyl)amino]methyl]-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxopyrrolidin-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxo-4-phenyl-pyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(1-hydroxy-1-methyl-ethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(4-acetamido-2-oxo-pyrrolidin-1-yl)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-[4-(methanesulfonamido)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-[4-[methyl(methylsulfonyl)amino]-2-oxo-pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(2,5-dioxopyrrolidin-1-yl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(2-oxopyrrolidin-1-yl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-methyl-N-[1-[(6S)-6-methyl-5-[(3,4,5-trifluorophenyl)carbamoyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-5-oxo-pyrrolidin-3-yl]oxazole-5-carboxamide;

N-methyl-N-[1-[(6S)-6-methyl-5-[(3,4,5-trifluorophenyl)carbamoyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-5-oxo-pyrrolidin-3-yl]oxazole-4-carboxamide;

N-methyl-N-[1-[(6S)-6-methyl-5-[(3,4,5-trifluorophenyl)carbamoyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-5-oxo-pyrrolidin-3-yl]oxazole-2-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(2-oxooxazolidin-3-yl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(3-oxomorpholin-4-yl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(5-methyl-2-oxo-oxazolidin-3-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(3-oxo-5,6,8,8a-tetrahydro-1H-imidazo[5,1-c][1,4]oxazin-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(3-oxo-5,6,8,8a-tetrahydro-1H-imidazo[5,1-c][1,4]oxazin-2-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(2-chloro-4-pyridyl)-3-(5,5-dimethyl-2-oxo-oxazolidin-3-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(5,5-dimethyl-2-oxo-oxazolidin-3-yl)-6-methyl-N-[2-(trifluoromethyl)-4-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(4-methyl-2-oxo-imidazolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[(4R)-2-oxo-4-phenyl-oxazolidin-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[(4S)-2-oxo-4-phenyl-oxazolidin-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxo-4-phenyl-imidazolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(4,4-dimethyl-2-oxo-imidazolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(5-oxo-4-oxa-6-azaspiro[2.4]heptan-6-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(6-oxo-5-oxa-7-azaspiro[3.4]octan-7-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

methyl 6-[(6S)-6-methyl-5-[(3,4,5-trifluorophenyl)carbamoyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-7-oxo-2,6-diazaspiro[3.4]octane-2-carboxylate;

ethyl 6-[(6S)-6-methyl-5-[(3,4,5-trifluorophenyl)carbamoyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-7-oxo-2,6-diazaspiro[3.4]octane-2-carboxylate;

(6S)-6-methyl-3-(5-methyl-2-oxo-pyrrolidin-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-(oxazole-2-carbonyl)-7-oxo-2,6-diazaspiro[3.4]octan-6-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(7-oxo-2-pyrimidin-2-yl-2,6-diazaspiro[3.4]octan-6-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxoindolin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(1-oxoisoindolin-2-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(5-oxo-7H-pyrrolo[3,4-b]pyridin-6-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(5-fluoropyrimidin-2-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(hydroxymethyl)pyrazol-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(methoxymethyl)pyrazol-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxo-5-phenyl-oxazolidin-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-5-(2-pyridyl)oxazolidin-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-5-(4-pyridyl)oxazolidin-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-5-(3-pyridyl)oxazolidin-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(5-oxazol-4-yl-2-oxo-oxazolidin-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(2-methyloxazol-5-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(2-methyloxazol-4-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(3-pyridyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(4-oxazol-4-yl-2-oxo-pyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(2-pyridyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(4-pyridyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxopyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(5-methyl-2-oxo-1-piperidyl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(4-cyano-2-oxo-pyrrolidin-1-yl)-N-[2-(difluoromethyl)-4-pyridyl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-cyano-4-(hydroxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(4-cyano-4-methyl-2-oxo-pyrrolidin-1-yl)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(hydroxymethyl)-4-methyl-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-[methyl(pyrimidin-2-yl)amino]-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxooxazolidin-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-6-methyl-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(2-chloro-4-pyridyl)-6-methyl-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxoimidazolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(2,2-dimethyl-5-oxo-morpholin-4-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[(3S)-3-methyl-5-oxo-morpholin-4-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-6-methyl-3-(2-oxoimidazolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(3-acetyl-5-oxo-imidazolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-3-(2,2-dimethyl-5-oxo-morpholin-4-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4R)-4-hydroxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4S)-4-hydroxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4S)-4-methoxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4R)-4-methoxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-3-[(4S)-4-methoxy-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[(4S)-2-oxo-4-pyrimidin-2-yloxy-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4S)-4-(5-fluoropyrimidin-2-yl)oxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-[2-hydroxyethyl(methyl)carbamoyl]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-[(2-hydroxy-1,1-dimethyl-ethyl)carbamoyl]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(morpholine-4-carbonyl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-[(3S)-3-hydroxypyrrolidine-1-carbonyl]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-[(3R)-3-hydroxypyrrolidine-1-carbonyl]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(3-hydroxyazetidine-1-carbonyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(dimethylcarbamoyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(pyrrolidine-1-carbonyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(oxazol-2-ylcarbamoyl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(2,2-dimethylmorpholine-4-carbonyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-[(2R)-2-methylmorpholine-4-carbonyl]-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-[(2S)-2-methylmorpholine-4-carbonyl]-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-[trans-2,6-dimethylmorpholine-4-carbonyl]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-[cis-2,6-dimethylmorpholine-4-carbonyl]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(3,3-difluoropyrrolidine-1-carbonyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-[methyl(oxazol-2-yl)carbamoyl]-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(3,3-difluoropyrrolidine-1-carbonyl)-4-methyl-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(4,4-difluoropiperidine-1-carbonyl)-4-methyl-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-methyl-4-(morpholine-4-carbonyl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-methyl-4-(5-methyl-1,3,4-oxadiazol-2-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-methyl-4-(1,3,4-oxadiazol-2-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-methyl-4-(3-methyl-1,2,4-oxadiazol-5-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-methyl-4-(5-methyl-1,2,4-oxadiazol-3-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[(2S)-2-oxazol-5-yl-5-oxo-morpholin-4-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[5-(3-methyl-1,2,4-oxadiazol-5-yl)-2-oxo-oxazolidin-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[5-(6-chloro-3-pyridyl)-2-oxo-oxazolidin-3-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[5-(5-fluoro-2-pyridyl)-2-oxo-oxazolidin-3-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[5-(6-fluoro-2-pyridyl)-2-oxo-oxazolidin-3-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(1-methylpyrazol-4-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxo-4-pyrimidin-5-yl-pyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-[(5-fluoropyrimidin-2-yl)amino]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[(4R)-2-oxo-4-pyrimidin-2-yloxy-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(3R,4R)-3,4-dihydroxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(3-hydroxy-4,4-dimethyl-2-oxo-pyrrolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxo-3H-pyrrolo[3,2-c]pyridin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(6-oxo-4,7-dihydropyrazolo[1,5-a]pyrazin-5-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(3-cyano-2-methyl-5-oxo-pyrrolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(5-hydroxy-2-oxo-1,3-oxazinan-3-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(7-oxo-6-azaspiro[3.4]octan-6-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(8-hydroxy-7-oxo-6-azaspiro[3.4]octan-6-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(7-hydroxy-6-oxo-5-azaspiro[2.4]heptan-5-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(6-methyl-2-oxo-1,3-oxazinan-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(4-methyl-2-oxo-1,3-oxazinan-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(3S,4R)-3,4-dihydroxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(3S,4R)-3-hydroxy-2-oxo-4-pyrimidin-2-yloxy-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[5-methyl-5-(morpholine-4-carbonyl)-2-oxo-1,3-oxazinan-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(2R,3R,4S)-4-hydroxy-2-methyl-5-oxo-3-pyrimidin-2-yloxy-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxo-4-pyrimidin-2-yl-pyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(3-hydroxy-2-oxo-4-phenyl-pyrrolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(5S)-5-methoxy-2-oxo-1,3-oxazinan-3-yl]-6-methyl-N-(3,4,5trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide; and

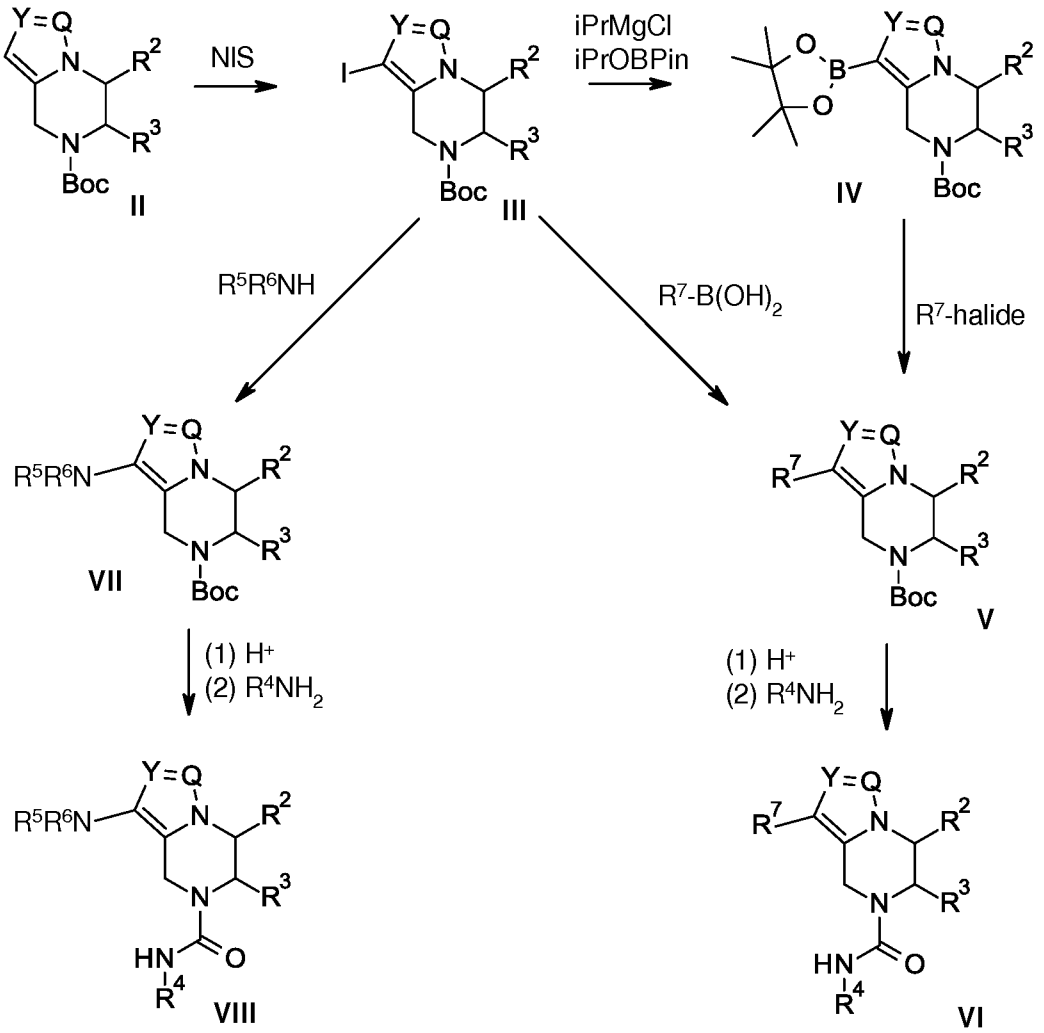
(6S)-3-[(5R)-5-methoxy-2-oxo-1,3-oxazinan-3-yl]-6-methyl-N-(3,4,5trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

SYNTHESIS

The compounds of the present invention can be prepared by any conventional means. Suitable processes for synthesizing these compounds as well as their starting materials are provided in the schemes below and in the examples. All substituents, in particular, R^1 to R^4 are as defined above unless otherwise indicated. Furthermore, and unless explicitly otherwise stated, all reactions, reaction conditions, abbreviations and symbols have the meanings well known to a person of ordinary skill in organic chemistry.

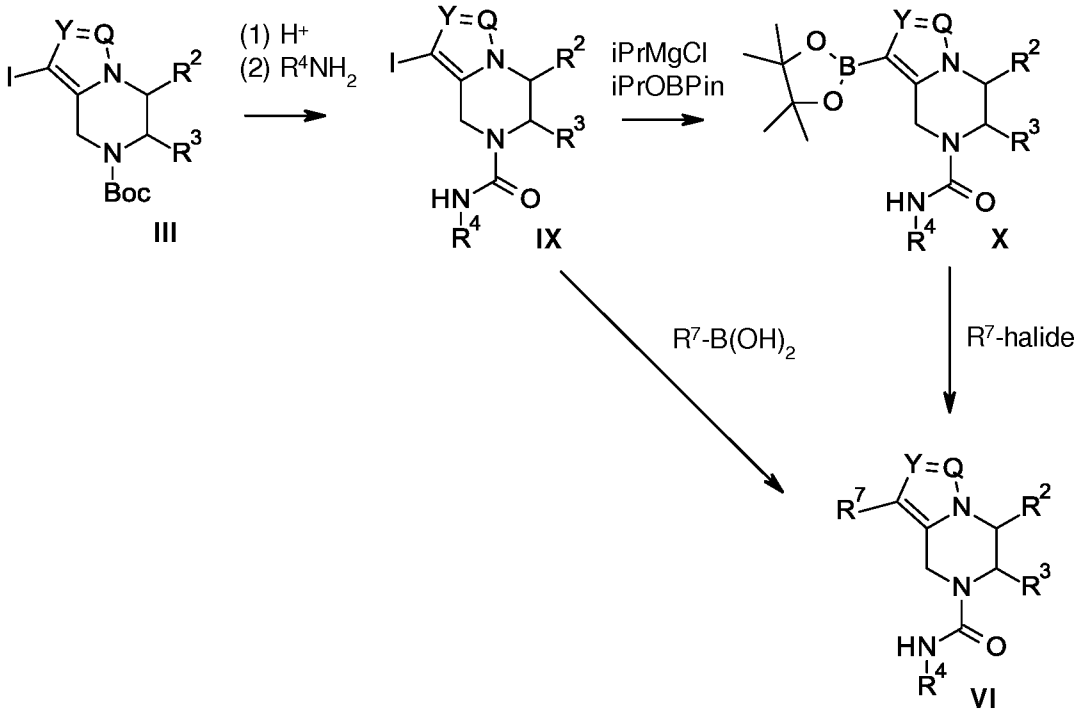
Scheme 1:



R^5 and R^6 are independently selected from H, C_{1-6}alkyl, heterocyclyl, C_{3-7}cycloalkyl, C_{1-6}alkylcarbonyl, heterocyclylcarbonyl and C_{3-7}cycloalkylcarbonyl; or R^5 and R^6 together with the nitrogen atom they are attached to form a 3-7 membered heterocyclyl, such as, but not limited to, pyrrolidinyl, piperidinyl, oxopyrrolidinyl, morpholinyl and oxomorpholinyl. R^7 is aryl or heteroaryl.

As depicted in **Scheme 1**, the synthesis of compounds of the present invention started from bicycle **II**, which was treated with iodinating reagents, such as N-iodosuccinimide, to give iodide **III**. Bicycle **II** was brominated with suitable brominating reagents, such as NBS, to give corresponding bromide, which was used in following reactions exemplified with iodide **III**. Palladium catalyzed Suzuki-Miyaura reaction between iodide **III** and boronic acid R^7-$B(OH)_2$ affords intermediate **V** (Buchwald, S. L. et al. *Acc Chem Res*. 2008, 41, 1461). Intermediated **V** was prepared from boronic acid pinacol ester **IV** and desired halide, R^1-halide, while boronic acid pinacol ester **IV** was prepared according to a known procedure (Bethel, P. A. et al. *Tetrahedron* 2012, 68, 5434) by reacting iodide **III** with Grignard reagent, such as iPrMgCl, and boronic ester, such as iPrOBPin. Deprotection of intermediate **V** in acidic conditions, such as HCl in EtOAc and TFA in DCM, followed by urea formation with amine R^4NH_2 in the presence of a phosgene equivalent, such as triphosgene and carbonyldiimidazole, affords final compound **VI**. In the aforementioned urea formation reaction, a suitable isocyanate or phenyl carbamate was used (Padiya, K. J. et al. *Org Lett*. 2012, 14, 2814 and references cited therein). On the other hand, copper catalyzed coupling reaction of iodide **III** with amine or amide R^5R^6NH afforded intermediate **VII**, which is then converted into final compound **VIII** by employing suitable urea formation methods mentioned above.

Scheme 2:

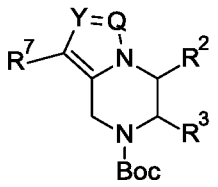


R^7 is aryl or heteroaryl.

Alternatively, compound **VI** was prepared according to synthetic route depicted in **Scheme 2**. That is, iodide **III** is first converted into urea **IX** by employing suitable urea formation methods mentioned above. Urea **IX** then reacted with boronic acid R^7-$B(OH)_2$ to give compound **VI** in the presence of palladium catalyst, or was converted to boronic ester **X** by known procedure mentioned above. Suzuki-Miyaura reaction of **X** with desired halide afforded compound **VI**.

This invention also relates to a process for the preparation of a compound of formula (I) comprising the reaction of:

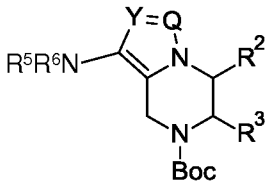
(a) the reaction of a compound of formula (V),



(V),

with an acid followed by urea formation with amine R^4NH_2 in the presence of a phosgene equivalent;

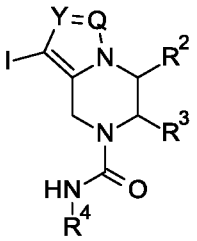
(b) the reaction of a compound of formula (VII),



(VII),

with an acid followed by urea formation with amine R^4NH_2 in the presence of a phosgene equivalent;

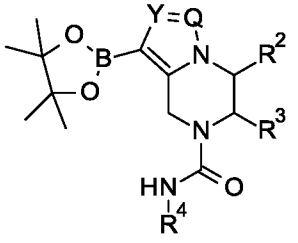
(c) the reaction of a compound of formula (IX),



(IX),

with R^7-$B(OH)_2$;

(d) the reaction of a compound of formula (X),



(X),

with halide via Suzuki-Miyaura reaction;

or wherein R^2, R^3 , R^4 are defined above; R^5 and R^6 are independently selected from H, C_{1-6}alkyl, C_{1-6}heteroalkyl, C_{3-6}cycloalkyl, C_{1-6}alkylcarbonyl, C_{1-6}heteroalkylcarbonyl, C_{3-6}cycloalkylcarbonyl and C_{3-6}heterocycloalkylcarbonyl; or R^5 and R^6 together with the nitrogen atom they are attached to form a 3-7 membered heterocyclyl, such as, but not limited to, pyrrolidinyl, piperidinyl, oxopyrrolidinyl, morpholinyl and oxomorpholinyl; R^7 is aryl or heteroaryl.

In step (a) and (b), the acid can be for example HCl in EtOAc and TFA in DCM; phosgene equivalent can be for example triphosgene and carbonyldiimidazole.

In step (d), the halide can be R^7-halide.

A compound of formula (I) when manufactured according to the above process is also an object of the invention.

PHARMACEUTICAL COMPOSITIONS AND ADMINISTRATION

Another embodiment provides pharmaceutical compositions or medicaments containing the compounds of the invention and a therapeutically inert carrier, diluent or excipient, as well as methods of using the compounds of the invention to prepare such compositions and medicaments. In one example, compounds of formula (I) may be formulated by mixing at ambient temperature at the appropriate pH, and at the desired degree of purity, with physiologically acceptable carriers, i.e., carriers that are non-toxic to recipients at the dosages and concentrations employed into a galenical administration form. The pH of the formulation depends mainly on the particular use and the concentration of compound, but preferably ranges anywhere from about 3 to about 8. In one example, a compound of formula (I) is formulated in an acetate buffer, at pH 5. In another embodiment, the compounds of formula (I) are sterile. The compound may be stored, for example, as a solid or amorphous composition, as a lyophilized formulation or as an aqueous solution.

Compositions are formulated, dosed, and administered in a fashion consistent with good medical practice. Factors for consideration in this context include the particular disorder being treated, the particular mammal being treated, the clinical condition of the individual patient, the cause of the disorder, the site of delivery of the agent, the method of administration, the scheduling of administration, and other factors known to medical practitioners. The "effective amount" of the compound to be administered will be governed by such considerations, and is the minimum amount necessary to the suppression of serum HBV DNA levels, or HBeAg seroconversion to HBeAb, or HBsAg loss, or normalization of alanine aminotransferase levels and improvement in liver histology. For example, such amount may be below the amount that is toxic to normal cells, or the mammal as a whole.

In one example, the pharmaceutically effective amount of the compound of the invention administered parenterally per dose will be in the range of about 0.01 to 100 mg/kg, alternatively about 0.1 to 20 mg/kg of patient body weight per day, with the typical initial range of compound used being 0.3 to 15 mg/kg/day. In another embodiment, oral unit dosage forms, such as tablets and capsules, contain from about 0.1 to about 1000 mg of the compound of the invention.

The compounds of the invention may be administered by any suitable means, including oral, topical (including buccal and sublingual), rectal, vaginal, transdermal, parenteral, subcutaneous, intraperitoneal, intrapulmonary, intradermal, intrathecal and epidural and intranasal, and, if desired for local treatment, intralesional administration. Parenteral infusions include intramuscular, intravenous, intraarterial, intraperitoneal, or subcutaneous administration.

The compounds of the present invention may be administered in any convenient administrative form, e.g., tablets, powders, capsules, solutions, dispersions, suspensions, syrups, sprays, suppositories, gels, emulsions, patches, etc. Such compositions may contain components conventional in pharmaceutical preparations, e.g., diluents, carriers, pH modifiers, sweeteners, bulking agents, and further active agents.

A typical formulation is prepared by mixing a compound of the present invention and a carrier or excipient. Suitable carriers and excipients are well known to those skilled in the art and are described in detail in, e.g., Ansel, Howard C., et al., Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems. Philadelphia: Lippincott, Williams & Wilkins, 2004; Gennaro, Alfonso R., et al. Remington: The Science and Practice of Pharmacy. Philadelphia: Lippincott, Williams & Wilkins, 2000; and Rowe, Raymond C. Handbook of Pharmaceutical Excipients. Chicago, Pharmaceutical Press, 2005. The formulations may also include one or more buffers, stabilizing agents, surfactants, wetting agents, lubricating agents, emulsifiers, suspending agents, preservatives, antioxidants, opaquing agents, glidants, processing aids, colorants, sweeteners, perfuming agents, flavoring agents, diluents and other known additives to provide an elegant presentation of the drug (i.e., a compound of the present invention or pharmaceutical composition thereof) or aid in the manufacturing of the pharmaceutical product (i.e., medicament).

An example of a suitable oral dosage form is a tablet containing about 0.1 mg to 1000 mg of the compound of the invention compounded with about 30 mg to 90 mg anhydrous lactose, about 5 mg to 40 mg sodium croscarmellose, about 5 mg to 30 mg polyvinylpyrrolidone (PVP) K30, and about 1 mg to 10 mg magnesium stearate. The powdered ingredients are first mixed together and then mixed with a solution of the PVP. The resulting composition can be dried, granulated, mixed with the magnesium stearate and compressed to tablet form using conventional equipment. An example of an aerosol formulation can be prepared by dissolving the compound, for example 5 mg to 400 mg, of the invention in a suitable buffer solution, e.g. a phosphate buffer, adding a tonicifier, e.g. a salt such sodium chloride, if desired. The solution may be filtered, e.g., using a 0.2 micron filter, to remove impurities and contaminants.

An embodiment, therefore, includes a pharmaceutical composition comprising a compound of formula (I), or a stereoisomer or pharmaceutically acceptable salt thereof. In a further embodiment includes a pharmaceutical composition comprising a compound of formula (I), or a

stereoisomer or pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or excipient.

INDICATIONS AND METHODS OF TREATMENT

The compounds of the invention can inhibit HBV's DNA synthesis and reduce HBV DNA levels. Accordingly, the compounds of the invention are useful for the treatment or prophylaxis of HBV infection.

The invention relates to the use of a compound of formula (I) for the treatment or prophylaxis of HBV infection.

The use of a compound of formula (I) for the preparation of medicaments useful in the treatment or prophylaxis diseases that are related to HBV infection is an object of the invention.

The invention relates in particular to the use of a compound of formula (I) for the preparation of a medicament for the treatment or prophylaxis of HBV infection.

Another embodiment includes a method for the treatment or prophylaxis of HBV infection which method comprises administering an effective amount of a compound of formula (I), a stereoisomer, tautomer, prodrug or pharmaceutically acceptable salt thereof.

EXAMPLES

The invention will be more fully understood by reference to the following examples. They should not, however, be construed as limiting the scope of the invention.

Abbreviations used herein are as follows:

DIPEA:	*N,N*-diisopropylethylamine
DCM:	dichloromethane
EA or EtOAc:	ethyl acetate
EC_{50}:	half maximal effective concentration
EDCI:	1-ethyl-3-(3-dimethylaminopropyl)carbodiimide
HATU:	1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxid hexafluorophosphate

HOBT:	hydroxybenzotriazole
HPLC:	high performance liquid chromatography
iPrOBPin:	2-isopropyl-4,4,5,5-tetramethyl-[1,3,2]dioxaborolane
LCMS	liquid chromatography–mass spectrometry
min(s):	minute(s)
MS:	mass spectrometry
MsCl:	methanesulfonyl chloride
NBS:	*N*-bromosuccinimide
NIS:	*N*-iodosuccinimide
PE:	petroleum ether
prep-HPLC:	preparative high performance liquid chromatography
prep-TLC:	preparative thin layer chromatography
SFC:	supercritical fluid chromatography
TEA:	triethylamine
pgRNA:	pre-genomic RNA
qPCR:	quantitative polymerase chain reaction
v/v	volume ratio

General Experimental Conditions

Intermediates and final compounds were purified by flash chromatography using one of the following instruments: i) Biotage SP1 system and the Quad 12/25 Cartridge module. ii) ISCO combi-flash chromatography instrument. Silica gel brand and pore size: i) KP-SIL 60 Å, particle size: 40-60 μm ; ii) CAS registry NO: Silica Gel: 63231-67-4, particle size: 47-60 micron silica gel; iii) ZCX from Qingdao Haiyang Chemical Co., Ltd, pore: 200-300 or 300-400.

Intermediates and final compounds were purified by preparative HPLC on reversed phase column using XBridge™ Prep-C18 (5 μm, OBDTM 30 × 100 mm) column or SunFire™ Prep-C18 (5 μm, OBD™ 30 × 100 mm) column. Waters AutoP purification System (Column: XBridge™ Prep-C18, 30 × 100 mm, Sample Manager 2767, Pump 2525, Detector: Micromass ZQ and UV 2487, solvent system: acetonitrile and 0.1% ammonium hydroxide in water). For SFC chiral separation, intermediates were separated by chiral column (Daicel chiralpak IC, 5 μm, 30 × 250 mm) using Mettler Toledo SFC-Multigram III system, solvent system: 95% CO_2 and 5% IPA (0.5% TEA in IPA), back pressure 100bar, detection UV@ 254nm.

LC/MS spectra of compounds were obtained using a LC/MS (Waters™ Alliance 2795-Micromass ZQ), LC/MS conditions were as follows (running time 6 mins):

Acidic condition: A: 0.1% formic acid in H_2O; B: 0.1% formic acid in acetonitrile;

Basic condition: A: 0.1% NH_3H_2O in H_2O; B: acetonitrile;

Neutral condition: A: H_2O; B: acetonitrile.

Mass spectra (MS): generally only ions which indicate the parent mass are reported, and unless otherwise stated the mass ion quoted is the positive mass ion $(MH)^+$.

NMR Spectra were obtained using Bruker Avance 400 MHz.

The microwave assisted reactions were carried out in a Biotage Initiator Sixty microwave synthesizer.

All reactions involving air-sensitive reagents were performed under an argon atmosphere. Reagents were used as received from commercial suppliers without further purification unless otherwise noted.

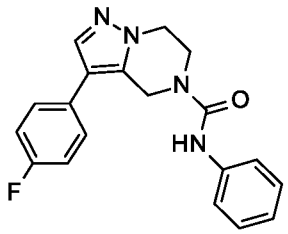
The following examples are intended to illustrate the meaning of the present invention but should by no means represent a limitation within the meaning of the present invention:

PREPARATIVE EXAMPLES

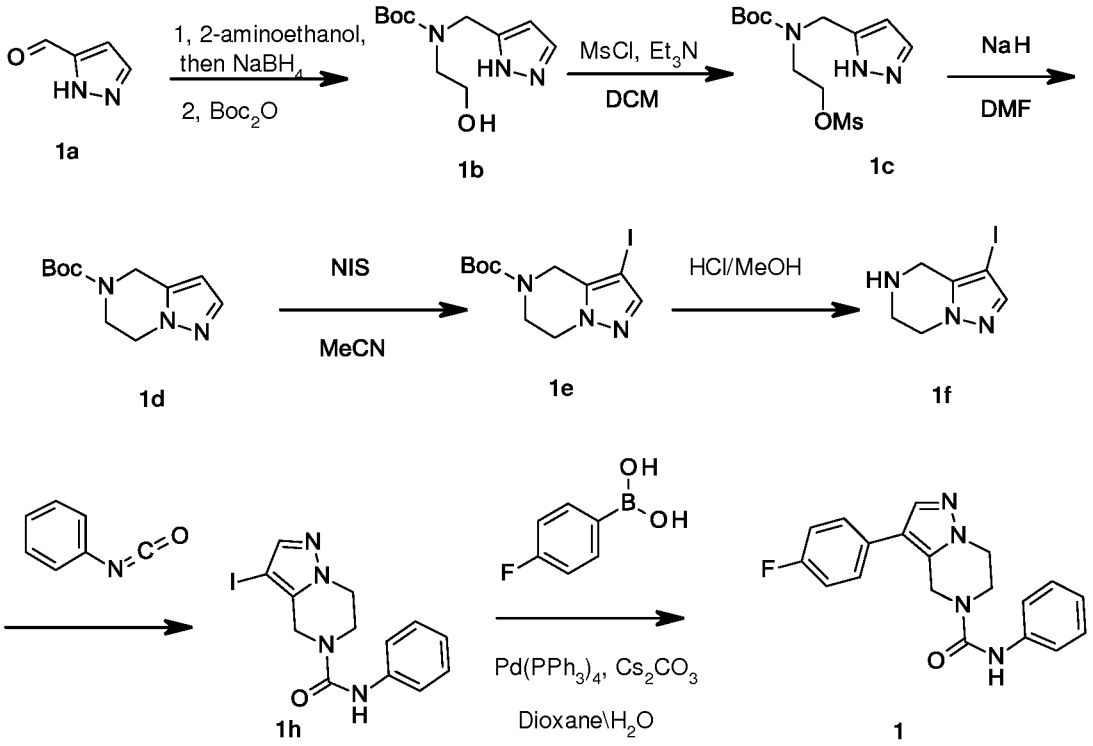
The invention will be more fully understood by reference to the following examples. They should not, however, be construed as limiting the scope of the invention.

Example 1:

3-(4-fluorophenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: preparation of tert-butyl N-(2-hydroxyethyl)-N-(1H-pyrazol-5-ylmethyl)carbamate (compound 1b)

To a solution of 1H-pyrazole-5-carbaldehyde (compound **1a**, 54.0 g, 562.5 mmol) in MeOH (300 mL) was added 2-aminoethanol (41.2 g, 675 mmol), and the reaction mixture was stirred at 25 °C for 1 hour. $NaBH_4$ (25.9 g, 675.0 mmol) was then added at 0 °C and the reaction mixture was stirred for another 1 hour. H_2O (300 mL) and Boc_2O (147.1 g, 675.0 mmol) were added to the reaction mixture, then the resulting mixture was stirred at room temperature for 12 hours, and extracted with EtOAc (600 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography (eluting with 20%~50% EtOAc in petroleum ether) to afford compound **1b** (80 g) as a colorless oil. LCMS ($M+H^+$): 320.

Step 2: preparation of 2-[tert-butoxycarbonyl(1H-pyrazol-5-ylmethyl)amino]ethyl methanesulfonate (compound 1c)

To a solution of tert-butyl N-(2-hydroxyethyl)-N-(1H-pyrazol-5-ylmethyl)carbamate (compound **1b**, 80.0 g, 117.2 mmol) and Et_3N (100.5 g, 995.6 mmol) in DCM (800 mL) was added MsCl (57.3 g, 497.8 mmol) slowly at 0 °C. The resulting mixture was stirred at room temperature for 2 hours, washed with water (500 mL), brine (500 mL) and dried over Na_2SO_4. The organic layer was concentrated to afford compound **1c** (100 g, crude), which was used directly in next step.

Step 3: preparation of tert-butyl 6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 1d)

To a solution of 2-[tert-butoxycarbonyl(1H-pyrazol-5-ylmethyl)amino]ethyl methanesulfonate (compound **1c**, 100.0 g, 313.4 mmol) in DMF (1000 mL) was added NaH (15.0 g, 376.2 mmol) in portions at 0 °C. The resulting mixture was stirred at room temperature for 12 hours, poured into water (2000 mL) and extracted with EtOAc (1000 mL) twice. The combined organic layer was dried over Na_2SO_4, and then concentrated to afford compound **1d** (18.0 g). LCMS ($M+H^+$): 224.

Step 4: preparation of tert-butyl 3-iodo-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 1e)

To a solution of tert-butyl 6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **1d**, 3.3 g, 14.8 mmol) in CH_3CN (40 mL) was added NIS (5.0 g, 22.1 mmol) slowly. The reaction mixture was stirred at room temperature for 16 hours and then diluted with EtOAc (50 mL), and washed with brine (50 mL). The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (eluting with 10%~80% EtOAc in petroleum ether) to afford compound **1e** (4.8 g) as a white solid. LCMS ($M+H^+$): 350. ^1H NMR (400 MHz, chloroform-d) δ ppm 7.53 (s, 1 H), 4.53 (br, 2 H), 4.20 (t, J = 5.27 Hz, 2 H), 3.89 (t, J =5.14 Hz, 2 H), 1.53 (s, 9 H).

Step 5: preparation of 3-iodo-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound 1f)

A solution of tert-butyl 3-iodo-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **1e**, 4.2 g, 12 mmol) in HCl/MeOH (30 mL) was stirred at room temperature for 3 hours. The reaction mixture was concentrated to afford compound **1f** (4 g) in HCl salt as a slight yellow solid. LCMS ($M+H^+$): 250.

Step 6: preparation of 3-iodo-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (compound 1h)

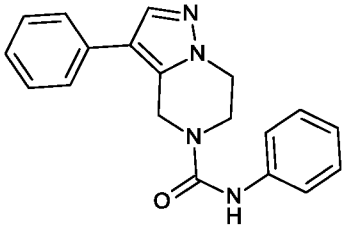
To a solution of 3-iodo-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **1f**, 4 g, 14 mmol) in DCM (40 mL) was added isocyanatobenzene (2.5 g, 21 mmol) and Et_3N (4.25 g, 42 mmol). The reaction mixture was stirred at room temperature for 1 hour, and then concentrated in *vacuo*. The residue was purified by column chromatography (eluting with 20%~50% EtOAc in petroleum ether) to afford compound **1h** as a white solid (4.8 g). LCMS ($M+H^+$): 369.

Step 7: preparation of 3-(4-fluorophenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 1):

To a solution of 3-iodo-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (compound **1h**, 0.1 g, 0.3 mmol) in dioxane/water (10 mL, 10:1, v/v) were added (4-fluorophenyl)boronic acid (40 mg, 0.3 mmol), $Pd(PPh_3)_4$ (10 mg, 0.1 mmol) and Cs_2CO_3 (195 mg, 0.6 mmol). The reaction mixture was stirred at 70 °C for 16 hours under nitrogen and then concentrated in *vacuo* to afford the crude product, which was purified by prep-HPLC to afford Example **1** as a white solid. LCMS ($M+H^+$): 337. ^1H NMR (400MHz, chloroform-d) δ ppm 7.70 (s, 1H), 7.40 - 7.30 (m, 6H), 7.17 - 7.08 (m, 3H), 6.45 (br. s, 1H), 4.88 (s, 2H), 4.37 (t, *J*=5.3 Hz, 2H), 4.05 (t, *J*=5.4 Hz, 2H).

Example 2:

N,3-diphenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

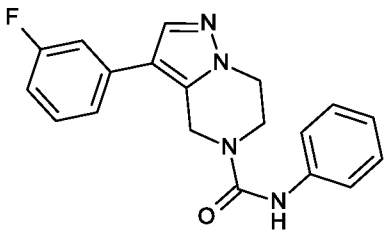


Preparation of Example 2:

The title compound was prepared in analogy to the preparation of Example **1** by using phenylboronic acid instead of (4-fluorophenyl)boronic acid. Example **2** was obtained as a white solid (30 mg). LCMS ($M+H^+$): 319. ^1H NMR (400MHz, DMSO-d_6) δ ppm 8.90 (s, 1H), 7.85 (s, 1H), 7.51-7.38 (m, 6H), 7.30-7.20 (m, 3H), 6.97 (m, 1H), 4.95 (s, 2H), 4.24 (m, 2H), 4.01 (m, 2H).

Example 3:

3-(3-fluorophenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



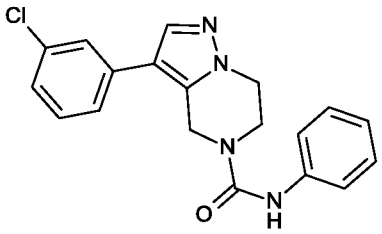
Preparation of Example 3:

The title compound was prepared in analogy to the preparation of Example **1** by using (3-fluorophenyl)boronic acid instead of (4-fluorophenyl)boronic acid. Example **3** was obtained as a white solid. LCMS ($M+H^+$): 337. 1H NMR (400MHz, chloroform-d) δ ppm 7.75 (s, 1H), 7.46 -

7.31 (m, 5H), 7.18 - 6.97 (m, 4H), 6.47 (s, 1H), 4.91 (s, 2H), 4.37 (t, *J*=5.3 Hz, 2H), 4.06 (t, *J*=5.4 Hz, 2H).

Example 4:

3-(3-chlorophenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

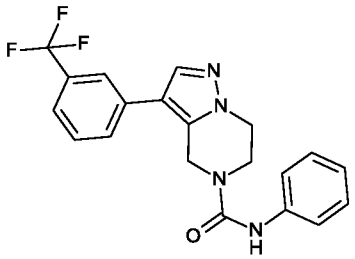


Preparation of Example 4:

The title compound was prepared in analogy to the preparation of Example **1** by using (3-chlorophenyl)boronic acid instead of (4-fluorophenyl)boronic acid. Example **4** was obtained as a white solid. LCMS ($M+H^+$): 353. ^1H NMR (400MHz, chloroform-d) δ ppm 7.75 (s, 1H), 7.41 - 7.29 (m, 7H), 7.25 (d, *J*=7.5 Hz, 1H), 7.13 (d, *J*=6.8 Hz, 1H), 6.48 (s, 1H), 4.91 (s, 2H), 4.38 (t, *J*=5.3 Hz, 2H), 4.06 (t, *J*=5.4 Hz, 2H).

Example 5:

N-phenyl-3-[3-(trifluoromethyl)phenyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

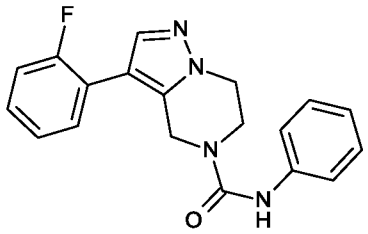


Preparation of Example 5:

The title compound was prepared in analogy to the preparation of Example **1** by using (3-trifluorophenyl)boronic acid instead of (4-fluorophenyl)boronic acid. Example **5** was obtained as a white solid. LCMS ($M+H^+$): 387. ^1H NMR (400MHz, CD_3OD) δ ppm 7.89 (s, 1H), 7.79 - 7.71 (m, 2H), 7.69 - 7.56 (m, 2H), 7.38 (d, *J*=8.0 Hz, 2H), 7.29 (t, J=7.9 Hz, 2H), 7.11 - 7.03 (m, 1H), 6.47 (s, 1H), 5.03 (s, 2H), 4.33 (t, *J*=5.4 Hz, 2H), 4.12 (t, *J*=5.3 Hz, 2H).

Example 6:

3-(2-fluorophenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

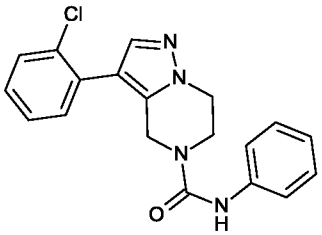


Preparation of Example 6:

The title compound was prepared in analogy to the preparation of Example **1** by using (2-fluorophenyl)boronic acid instead of (4-fluorophenyl)boronic acid. Example **6** was obtained as a white solid. LCMS ($M+H^+$): 337. ^1H NMR (400MHz, chloroform-d) ppm 7.76 (s, 1H), 7.35 (m, 6H), 7.26 - 7.16 (m, 2H), 7.11 (t, *J*=6.9 Hz, 1H), 6.47 (s, 1H), 4.81 (s, 2H), 4.40 (t, *J*=5.4 Hz, 2H), 4.09 (t, *J*=5.4 Hz, 2H).

Example 7:

3-(2-chlorophenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

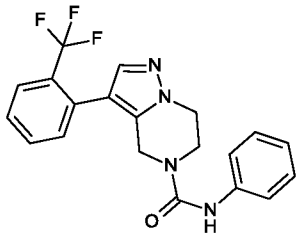


Preparation of Example 7:

The title compound was prepared in analogy to the preparation of Example **1** by using (2-chlorophenyl)boronic acid instead of (4-fluorophenyl)boronic acid. Example **7** was obtained as a white solid . LCMS ($M+H^+$): 353. ^1H NMR (400MHz, chloroform-d) δ ppm 7.70 (s, 1H), 7.55 - 7.49 (m, 1H), 7.38 - 7.29 (m, 7H), 7.11 (d, *J*=5.8 Hz, 1H), 6.45 (br. s, 1H), 4.74 (s, 2H), 4.42 (t, *J*=5.3 Hz, 2H), 4.09 (t, *J*=5.3 Hz, 2H).

Example 8:

N-phenyl-3-[2-(trifluoromethyl)phenyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

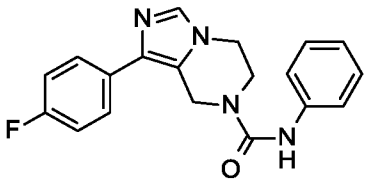


Preparation of Example 8:

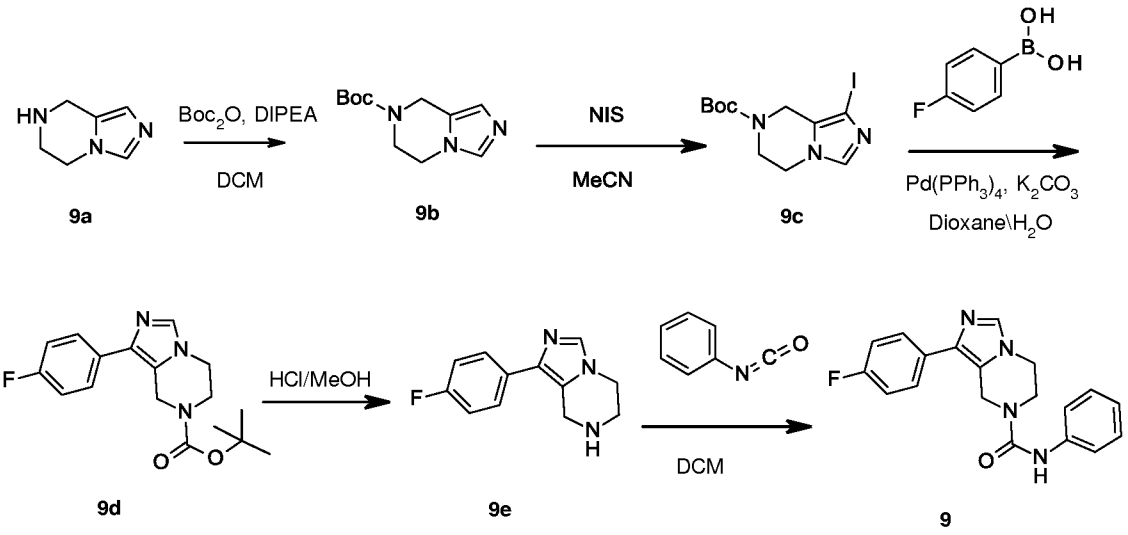
The title compound was prepared in analogy to the preparation of Example **1** by using (2-trifluorophenyl)boronic acid instead of (4-fluorophenyl)boronic acid. Example **8** was obtained as a white solid . LCMS ($M+H^+$): 387. ^1H NMR (400MHz, chloroform-d) δ ppm 7.81 (d, *J*=7.5 Hz, 1H), 7.64 - 7.50 (m, 3H), 7.36 - 7.29 (m, 5H), 7.10 (s, 1H), 6.33 (s, 1H), 4.59 (s, 2H), 4.39 (t, *J*=5.4 Hz, 2H), 4.06 (t, *J*=5.5 Hz, 2H).

Example 9:

1-(4-fluorophenyl)-N-phenyl-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide



The title compound was prepared according to the following scheme:



Step 1: **preparation of tert-butyl 6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxylate (compound 9b)**

To a solution of 5,6,7,8-tetrahydroimidazo[1,5-a]pyrazine (compound **9a**, 3.7 g, 30 mmol) and DIPEA (11.6 g, 90 mmol) in DCM (50 mL) was added Boc_2O (7.2 g, 33 mmol) at 0 °C. The

resulting mixture was stirred at room temperature for 12 hours, and then concentrated and purified by column chromatography (eluting with 30%~100% EtOAc in petroleum ether) to afford compound **9b** (4.7 g) as a white solid. LCMS ($M+H^+$): 224.

Step 2: **preparation of tert-butyl 1-iodo-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxylate (compound 9c)**

To a solution of tert-butyl 6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxylate a]pyrazine (compound **9b,** 4.6 g, 21 mmol) in CH_3CN (50 mL) was added NIS (5.6 g, 2.5 mmol) and then the reaction mixture was stirred at room temperature for 48 hours and then concentrated and the residue was purified by column chromatography (eluting with 10%~80% EtOAc in petroleum ether) to afford compound **9c** (5 g) as a yellow solid. LCMS ($M+H^+$): 350.

Step 3: **preparation of tert-butyl 1-(4-fluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxylate (compound 9d)**

To a mixture of tert-butyl 1-iodo-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxylate (compound **9c**, 1.1 g, 3 mmol), (4-fluorophenyl)boronic acid (630 mg, 4.5 mmol) and K_2CO_3 (1.2 g, 9 mmol) in dioxane/water (10 mL, 5:1, v/v) was added $Pd(PPh_3)_4$ (150 mg, 0.015 mmol) under N_2. The reaction mixture was stirred at 80 °C for 12 hours, and then concentrated. The residue was purified by column chromatography (eluting with 10%~50% EtOAc in petroleum ether) to afford compound **9d** (550 mg). LCMS ($M+H^+$): 318.

Step 4: preparation of 1-(4-fluorophenyl)-5,6,7,8-tetrahydroimidazo[1,5-a]pyrazine (compound 9e)

A solution of tert-butyl 1-(4-fluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxylate (compound **9d**, 550 mg, 1.7 mmol) in HCl/MeOH (20 mL) was stirred at room temperature for 2 hours. Then the reaction mixture was concentrated in *vacuo* to afford compound **9e** (400 mg) as a slight yellow solid, which was used directly without further purification in next step. LCMS ($M+H^+$): 236.

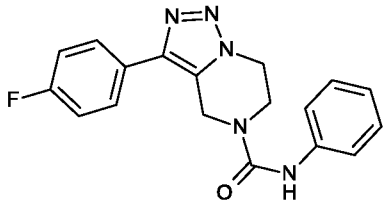
Step 5: preparation of 1-(4-fluorophenyl)-N-phenyl-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide (Example 9)

To a solution of **1**-(4-fluorophenyl)-5,6,7,8-tetrahydroimidazo[1,5-a]pyrazine (compound **9e,** 88 mg, 0.4 mmol) and Et_3N (204 mg, 2.0 mmol) in DCM (5 mL) was added isocyanatobenzene (96 mg, 0.8 mmol) and then the reaction mixture was stirred at room temperature for 30 min. The solvent was removed in *vacuo* and the residue was purified by prep-HPLC to afford 1-(4-fluorophenyl)-N-phenyl-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide (Example **9**, 20 mg) as a white solid. LCMS ($M+H^+$): 337. ^1H NMR (400MHz,

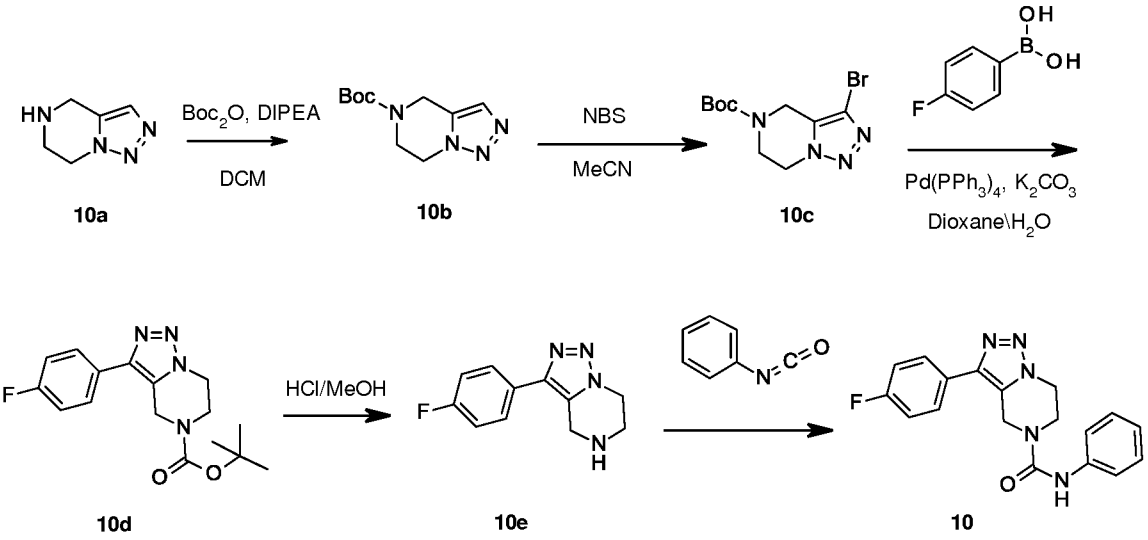
DMSO-d_6) δ ppm 8.85 (s, 1H), 7.75 (s, 1H), 7.71 - 7.62 (m, 2H), 7.48 - 7.44 (m, 2H), 7.29 - 7.22 (m, 4H), 7.04 - 6.92 (m, 1H), 4.95 (s, 2H), 4.18 - 4.14 (m, 2H), 3.92 - 3.88 (m, 2H).

Example 10:

3-(4-fluorophenyl)-N-phenyl-6,7-dihydro-4H-triazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: **preparation of tert-butyl 6,7-dihydro-4H-triazolo[1,5-a]pyrazine-5-carboxylate (compound 10b)**

To a solution of 4,5,6,7-tetrahydrotriazolo[1,5-a]pyrazine (compound **10a**, 3.7 g, 30 mmol) and DIPEA (11.6 g, 90 mmol) in DCM (50 mL) was added Boc_2O (7.2 g, 33 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for 12 hours. The reaction mixture was concentrated and the residue purified by column chromatography (eluting with 30%~100% EtOAc in petroleum ether) to afford compound **10b** (4.7 g) as a white solid. LCMS ($M+H^+$): 225.

Step 2: **preparation of tert-butyl 3-bromo-6,7-dihydro-4H-triazolo[1,5-a]pyrazine-5-carboxylate (compound 10c)**

To a solution of tert-butyl 6,7-dihydro-4H-triazolo[1,5-a]pyrazine-5-carboxylate (compound **10b**, 4.6 g, 21 mmol) in CH_3CN (50 mL) was added N-bromosuccinimide (NBS, 5.6 g, 2.5 mmol) and then the reaction mixture was stirred at room temperature for 48 hours. The

reaction mixture was concentrated and the residue was purified by column chromatography (eluting with 10%~80% EtOAc in petroleum ether) to afford compound **10c** (5 g) as a yellow solid. LCMS ($M+H^+$): 351.

Step 3: **preparation of tert-butyl 3-(4-fluorophenyl)-6,7-dihydro-4H-triazolo[1,5-a]pyrazine-5-carboxylate (compound 10d)**

To a mixture of tert-butyl 3-bromo-6,7-dihydro-4H-triazolo[1,5-a]pyrazine-5-carboxylate (compound **10c**, 1.1 g, 3 mmol), (4-fluorophenyl)boronic acid (630 mg, 4.5 mmol) and K_2CO_3 (1.2 g, 9 mmol) in dioxane/water (10 mL, 5:1, v/v) was added $Pd(PPh_3)_4$ (150 mg) under N_2. The reaction mixture was stirred at 80 °C for 16 hours. Then the reaction was concentrated and the residue was purified by column chromatography (eluting with 10%~50% EtOAc in petroleum ether) to afford compound **10d** (550 mg). LCMS ($M+H^+$): 319.

Step 4: preparation of 3-(4-fluorophenyl)-4,5,6,7-tetrahydrotriazolo[1,5-a]pyrazine (compound 10e)

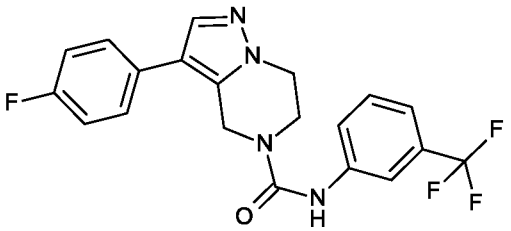
A solution of tert-butyl 3-(4-fluorophenyl)-6,7-dihydro-4H-triazolo[1,5-a]pyrazine-5-carboxylate (compound **10d**, 550 mg, 1.7 mmol) in HCl/MeOH (20 mL) was stirred at room temperature for 2 hours. Then the reaction mixture was concentrated in *vacuo* to afford compound **10e** (400 mg) as a slight yellow solid. LCMS ($M+H^+$): 219.

Step 5: preparation of 3-(4-fluorophenyl)-N-phenyl-6,7-dihydro-4H-triazolo[1,5-a]pyrazine-5-carboxamide (Example 10)

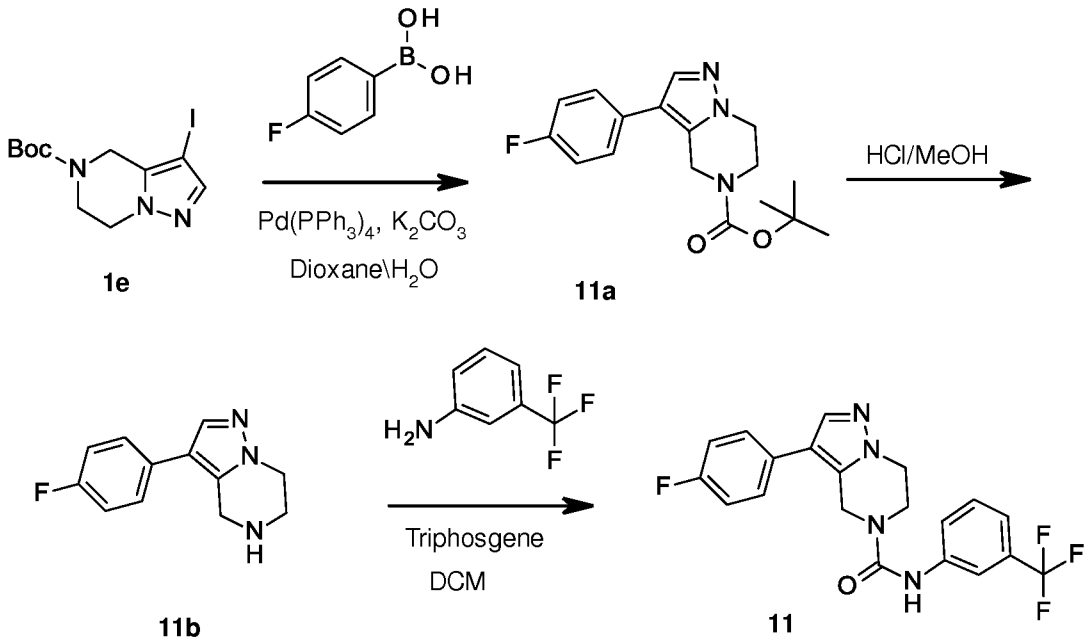
The title compound was prepared in analogy to the preparation of Example **9** by using 3-(4-fluorophenyl)-4,5,6,7-tetrahydrotriazolo[1,5-a]pyrazine (compound **10e**) instead of 1-(4-fluorophenyl)-5,6,7,8-tetrahydroimidazo[1,5-a]pyrazine (compound **9e**). Example **10** was obtained as a white solid (45 mg). LCMS ($M+H^+$): 338. ^1H NMR (400MHz, DMSO-d_6) δ ppm 8.92 (s, 1H), 7.83 - 7.76 (m, 2H), 7.46 (d, *J*=7.5 Hz, 2H), 7.36 (t, *J*=8.8 Hz, 2H), 7.27 (t, *J*=7.9 Hz, 2H), 7.03 - 6.96 (m, 1H), 5.05 (s, 2H), 4.51 (t, *J*=5.3 Hz, 2H), 4.03 (t, *J*=5.3 Hz, 2H).

Example 11:

3-(4-fluorophenyl)-N-[3-(trifluoromethyl)phenyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: **preparation of tert-butyl 3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 11a)**

To a mixture of tert-butyl 3-iodo-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **1e**, 1.1 g, 3 mmol), (4-fluorophenyl)boronic acid (630 mg, 4.5 mmol) and K_2CO_3 (1.2 g, 9 mmol) in and dioxane/water (10 mL, 5:1, v/v) was added $Pd(PPh_3)_4$ (150 mg) under N_2. The reaction mixture was stirred at 80 °C for 2 hours. Then the reaction was concentrated and the residue was purified by column chromatography to afford compound **11a** (550 mg) as a slight yellow solid. LCMS ($M+H^+$): 318.

Step 2: preparation of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound 11b)

A solution of tert-butyl 3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **11a**, 550 mg, 1.7 mmol) in HCl/MeOH (20 mL) was stirred at room temperature for 2 hours. Then the reaction mixture was concentrated in *vacuo* to afford compound **11b** (400 mg) as a slight yellow solid. LCMS ($M+H^+$): 218.

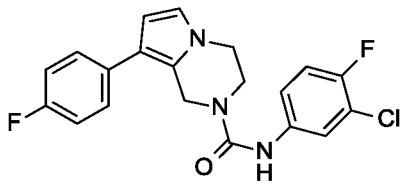
Step 3: preparation of N-(2-fluorophenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 11)

To a mixture of 3-(trifluoromethyl)aniline (64 mg) and DIPEA (0.1 mL) in DCM (5 mL) was added triphosgene (36 mg). After stirring for 10 min at room temperature, 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**, 50 mg) was added to

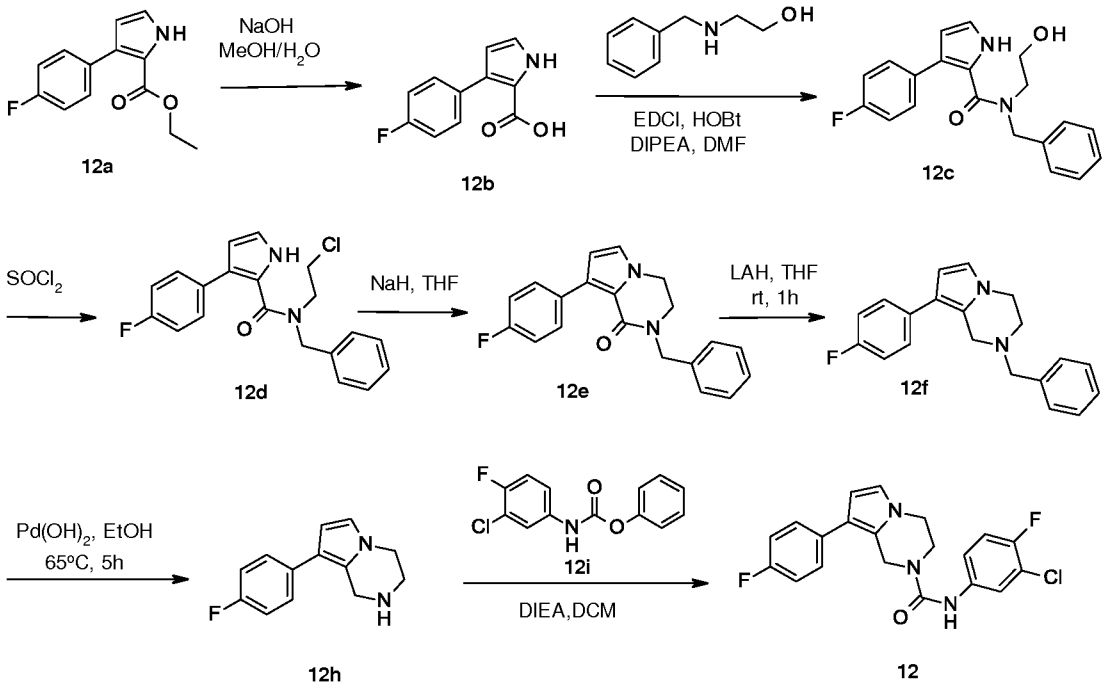
the reaction mixture. The resulting mixture was stirred at room temperature for 12 hours, then diluted with EtOAc (10 mL), washed with water (5 mL) and brine (5 mL). The organic layer was concentrated and the residue was purified by prep-HPLC to afford Example **11** (50 mg) as a white solid. LCMS ($M+H^+$): 405. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.21 (s, 1H), 7.90 (s, 1H), 7.84 (s, 1H), 7.74 (d, *J*=8.0 Hz, 1H), 7.54 - 7.46 (m, 3H), 7.35 - 7.22 (m, 3H), 4.95 (s, 2H), 4.24 (t, *J*=5.0 Hz, 2H), 4.02 (t, *J*=5.1 Hz, 2H).

Example 12:

N-(3-chloro-4-fluoro-phenyl)-8-(4-fluorophenyl)-3,4-dihydro-1H-pyrrolo[1,2-a]pyrazine-2-carboxamide



The title compound was prepared according to the following scheme:



Step 1: preparation of 3-(4-fluorophenyl)-1H-pyrrole-2-carboxylic acid (compound 12b):

To a solution of 8-(4-fluorophenyl)-1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazine (compound **12a**, 2.9 g, 12.4 mmol) (for its synthesis, refer to: Liu, J. et al, *Angew Chem Int. Ed.*, 2013, 52, 6953) in MeOH (13.5 mL) were added sequentially H_2O (4.5 mL) and NaOH (750 mg, 18.6

mmol). The reaction mixture was stirred at 75 °C for 5 hours, then cooled down, quenched by adding ice-water, neutralized to pH 6.0 with 1.0 N HCl solution in methanol, extracted with EtOAc/THF (60 mL, 5/2, v/v). The organic layer was dried over Na_2SO_4, filtered and concentrated to give compound **12b** (2.5 g) as a crude product, which was used directly in next step. LCMS ($M+H^+$): 206.

Step 2: preparation of N-benzyl-3-(4-fluorophenyl)-N-(2-hydroxyethyl)-1H-pyrrole-2-carboxamide (compound 12c):

To a solution of 3-(4-fluorophenyl)-1H-pyrrole-2-carboxylic acid (compound **12b**, 2.5 g, 12.4 mmol) in DMF (10 mL) were added 2-(benzylamino)ethanol (2.3 g, 15.0 mmol), EDCI (3.1 g, 16.1 mmol), HOBt (0.5 g, 3.7 mmol) and DIPEA (3.0 mL). The reaction mixture was stirred at room temperature overnight, quenched by adding ice-water, then extracted with EtOAc (60 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography (eluting with 40%~60% EtOAc in petroleum ether) to afford compound **12c** (3.0 g) as a white solid. LCMS ($M+H^+$): 339.

Step 3: preparation of N-benzyl-N-(2-chloroethyl)-3-(4-fluorophenyl)-1H-pyrrole-2-carboxamide (compound 12d):

To a solution of N-benzyl-3-(4-fluorophenyl)-N-(2-hydroxyethyl)-1H-pyrrole-2-carboxamide (compound **12c**, 676 mg, 2.0 mmol) in dioxane (8.0 mL) was added dropwise thionyl chloride (435 μL, 6.0 mmol). The resulting mixture was stirred at room temperature for 2 hours, and then quenched by adding ice-water, extracted with EtOAc/petroleum ether (50 mL, 1/1, v/v) twice. The organic layer was dried over Na_2SO_4, filtered and concentrated to give crude compound **12d** (712 mg) which was used directly in next step. LCMS ($M+H^+$): 357.

Step 4: preparation of 2-benzyl-8-(4-fluorophenyl)-3,4-dihydropyrrolo[1,2-a]pyrazin-1-one (compound 12e):

To a solution of N-benzyl-N-(2-chloroethyl)-3-(4-fluorophenyl)-1H-pyrrole-2-carboxamide (compound **12d**, 712 mg, 2.0 mmol) in dry THF (10 mL) was added sodium hydride (60% dispersion in mineral oil, 120 mg, 3.0 mmol). The reaction mixture was stirred at room temperature for 1 hour, diluted with THF (50 mL), and quenched with sodium sulfate decahydrate. The resulting mixture was stirred at room temperature for 1 hour, then filtered and concentrated. The residue was purified by column chromatography (eluting with 25%~35% EtOAc in petroleum ether) to afford compound **12e** (512 mg) as a white solid. LCMS ($M+H^+$): 321.

Step 5: preparation of 2-benzyl-8-(4-fluorophenyl)-3,4-dihydro-1H-pyrrolo[1,2-a]pyrazine (compound 12f):

A solution of 2-benzyl-8-(4-fluorophenyl)-3,4-dihydropyrrolo[1,2-a]pyrazin-1-one (compound **12e**, 96 mg, 0.3 mmol) in THF (2.0 mL) was added lithium aluminum hydride (12 mg, 0.3 mmol) and stirred at room temperature for 1 hour. The reaction mixture was diluted with THF (30 mL), quenched by adding sodium sulfate decahydrate. The resulting mixture was stirred at room temperature for 1 hour, then filtered and concentrated to give crude compound **12f** (92 mg) which was used directly in next step . LCMS ($M+H^+$): 307.

Step 6: preparation of 8-(4-fluorophenyl)-1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazine (compound 12h):

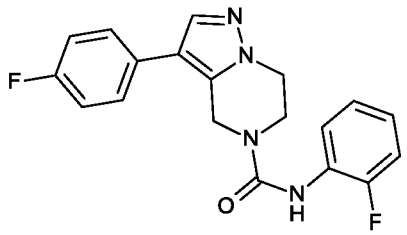
To a solution of 2-benzyl-8-(4-fluorophenyl)-3,4-dihydro-1H-pyrrolo[1,2-a]pyrazine (compound **12f**, 640 mg, 2.0 mmol) in EtOH (20 mL) was added palladium hydroxide (20% on carbon, wetted with ca. 50% water, 0.5 g). The reaction mixture was heated to reflux under 1 atm. H_2 overnight. After cooled to room temperature, the reaction mixture was filtered and concentrated to give crude compound **12h** (432 mg) which was used directly in next step. LCMS ($M+H^+$): 217.

Step 7: preparation of N-(3-chloro-4-fluoro-phenyl)-8-(4-fluorophenyl)-3,4-dihydro-1H-pyrrolo[1,2-a]pyrazine-2-carboxamide (Example 12):

To a solution of 8-(4-fluorophenyl)-1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazine (compound **12h**, 54 mg, 0. 25 mmol) in DCM (2.0 mL) was added DIPEA (0.1 mL), phenyl N-(3-chloro-4-fluoro-phenyl)carbamate (compound **12i**, 80 mg, 0.3 mmol) (for its synthesis, refer to: Sheng, C. et al, *Eur. J. Med. Chem.* 2011, 46, 5276). The reaction mixture was stirred at 40 °C for 3 hours. The reaction mixture was concentrated in *vacuo* to give the crude product, which was purified by prep-HPLC to afford Example **12** (10 mg). LCMS ($M+H^+$): 388. ^1H NMR (400MHz, CD_3OD) δ ppm 7.59 (dd, *J*=2.5, 6.8 Hz, 1H), 7.43 - 7.35 (m, 2H), 7.33 - 7.27 (m, 1H), 7.18 - 7.07 (m, 3H), 6.75 (d, *J*=2.8 Hz, 1H), 6.33 (d, *J*=2.8 Hz, 1H), 4.88 (s, 2H), 4.12 (d, *J*=4.5 Hz, 2H), 3.94 (d, *J*=5.8 Hz, 2H).

Example 13:

N-(2-fluorophenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

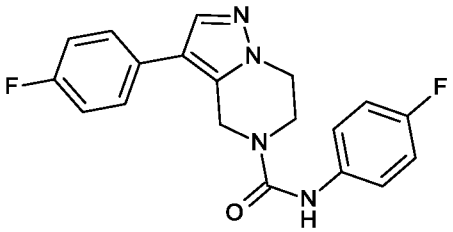


Preparation of Example 13:

The title compound was prepared in analogy to the preparation of Example **9** by using 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**, 50mg) instead of 1-(4-fluorophenyl)-5,6,7,8-tetrahydroimidazo[1,5-a]pyrazine (compound **9e**), and 1-fluoro-2-isocyanato-benzene (44 mg) instead of isocyanatobenzene. Example **13** was obtained as a white solid (40 mg). LCMS ($M+H^+$): 355. ^1H NMR (400MHz, DMSO-d_6) δ ppm 8.92 (s, 1H), 7.83 (s, 1H), 7.53 - 7.42 (m, 4H), 7.27 (t, *J*=8.9 Hz, 2H), 7.14 - 7.06 (m, 2H), 4.92 (s, 2H), 4.22 (t, *J*=5.3 Hz, 2H), 4.04 - 3.96 (m, 2H).

Example 14:

N,3-bis(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

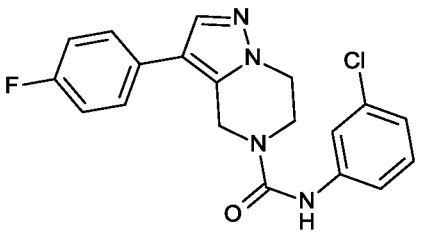


Preparation of Example 14:

The title compound was prepared in analogy to the preparation of Example **11** by using 4-fluoroaniline instead of 3-(trifluoromethyl)aniline. Example **14** was obtained as a white solid (20 mg). LCMS ($M+H^+$): 355. ^1H NMR (400MHz, DMSO-d_6) δ ppm 8.92 (s, 1H), 7.83 (s, 1H), 7.54 - 7.40 (m, 4H), 7.27 (t, *J*=8.9 Hz, 2H), 7.16 - 7.04 (m, 2H), 4.92 (s, 2H), 4.22 (t, *J*=5.3 Hz, 2H), 4.04 - 3.95 (m, 2H).

Example 15:

N-(3-chlorophenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

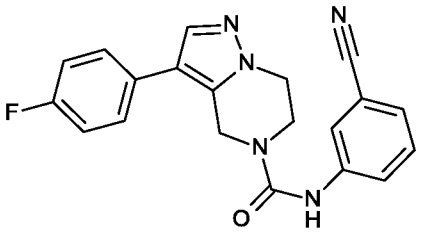


Preparation of Example 15:

The title compound was prepared in analogy to the preparation of Example **11** by using 3-chloroaniline instead of 3-(trifluoromethyl)aniline. Example **15** was obtained as a white solid . LCMS ($M+H^+$): 371. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.06 (s, 1H), 7.84 (s, 1H), 7.63 (s, 1H), 7.53 - 7.45 (m, 2H), 7.41 (d, *J*=8.3 Hz, 1H), 7.33 - 7.23 (m, 3H), 7.02 (d, *J*=7.8 Hz, 1H), 4.94 (s, 2H), 4.23 (m, 2H), 4.00 (m, 2H).

Example 16:

N-(3-cyanophenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

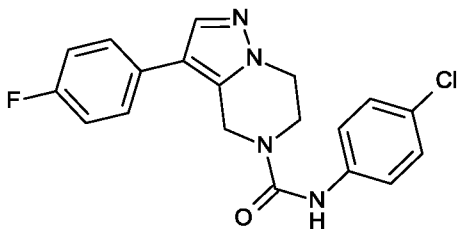


Preparation of Example 16:

The title compound was prepared in analogy to the preparation of Example **11** by using 3-aminobenzonitrile instead of 2-fluoroaniline. Example **16** was obtained as a white solid (30 mg). LCMS ($M+H^+$): 362. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.21 (s, 1H), 7.92 (s, 1H), 7.84 (s, 1H), 7.76 (d, *J*=8.0 Hz, 1H), 7.54 - 7.39 (m, 4H), 7.32 - 7.22 (m, 2H), 4.95 (s, 2H), 4.24 (m, 2H), 4.02 (m, 2H).

Example 17:

N-(4-chlorophenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

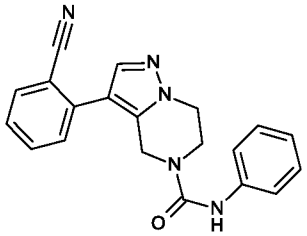


Preparation of Example 17:

The title compound was prepared in analogy to the preparation of Example **11** by using 4-chloroaniline instead of 3-(trifluoromethyl)aniline. Example **17** was obtained as a white solid (30 mg). LCMS ($M+H^+$): 371. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.00 (s, 1H), 7.83 (s, 1H), 7.49 (d, *J*=8.3 Hz, 4H), 7.37 - 7.22 (m, 4H), 4.93 (s, 2H), 4.27 - 4.17 (m, 2H), 4.01 (d, *J*=4.8 Hz, 2H).

Example 18:

3-(2-cyanophenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

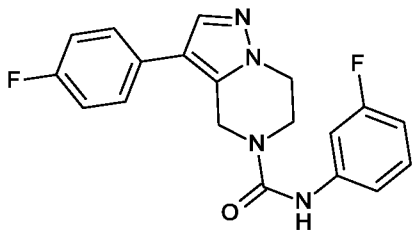


Preparation of Example 18:

The title compound was prepared in analogy to the preparation of Example **1** by using (2-cyanophenyl)boronic acid instead of (4-fluorophenyl)boronic acid. Example **18** was obtained as a white solid (20 mg). LCMS ($M+H^+$): 344. ^1H NMR (400MHz, DMSO-d_6) δ ppm 8.86 (s, 1H), 7.94 (d, *J*=7.5 Hz, 1H), 7.84 (s, 1H), 7.78 (t, *J*=7.5 Hz, 1H), 7.59 - 7.40 (m, 4H), 7.29 - 7.20 (m, 2H), 7.01 - 6.92 (m, 1H), 4.84 (s, 2H), 4.28 (t, *J*=5.0 Hz, 2H), 4.03 (t, *J*=5.1 Hz, 2H).

Example 19:

N-(3-fluorophenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

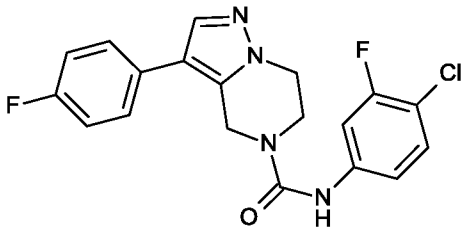


Preparation of Example 19:

The title compound was prepared in analogy to the preparation of Example **11** by using 3-fluoroaniline instead of 2-fluoroaniline. Example **19** was obtained as a white solid (30 mg). LCMS ($M+H^+$): 355. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.14 - 9.01 (m, 1H), 7.83 (s, 1H), 7.50 (dd, *J*=5.6, 8.2 Hz, 2H), 7.42 (d, *J*=12.0 Hz, 1H), 7.35 - 7.18 (m, 4H), 6.78 (t, *J*=7.8 Hz, 1H), 4.93 (s, 2H), 4.28 - 4.17 (m, 2H), 4.01 (d, *J*=5.3 Hz, 2H).

Example 20:

N-(4-chloro-3-fluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

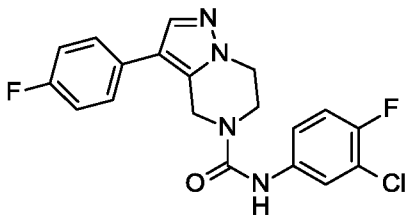


Preparation of Example 20:

The title compound was prepared in analogy to the preparation of Example **11** by using 4-chloro-3-fluoro-aniline instead of 3-(trifluoromethyl)aniline. Example **20** was obtained as a white solid. LCMS ($M+H^+$): 389. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.20 (s, 1H), 7.83 (s, 1H), 7.70 - 7.57 (m, 1H), 7.53 - 7.40 (m, 3H), 7.35 - 7.21 (m, 3H), 4.93 (s, 2H), 4.30 - 4.15 (m, 2H), 4.01 (d, *J*=4.8 Hz, 2H).

Example 21:

N-(3-chloro-4-fluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



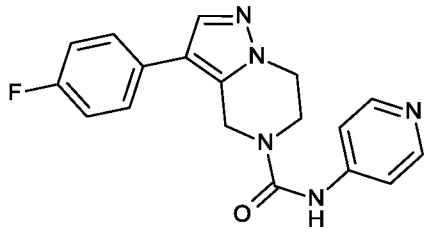
Preparation of Example 21:

The title compound was prepared in analogy to the preparation of Example **11** by using 3-chloro-4-fluoro-aniline instead of 3-(trifluoromethyl)aniline. Example **21** was obtained as a white solid (32 mg). LCMS ($M+H^+$): 389. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.05 (s, 1H),

7.83 (s, 1H), 7.72 (dd, *J*=2.3, 6.8 Hz, 1H), 7.49 (dd, *J*=5.5, 8.5 Hz, 2H), 7.44 - 7.38 (m, 1H), 7.30 (td, *J*=9.0, 18.2 Hz, 3H), 4.93 (s, 2H), 4.22 (t, *J*=5.0 Hz, 2H), 4.06 - 3.95 (m, 2H).

Example 22:

3-(4-fluorophenyl)-N-(4-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

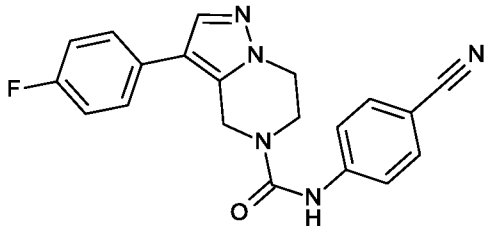


Preparation of Example 22:

The title compound was prepared in analogy to the preparation of Example **11** by using 4-amino-pyridine instead of 3-(trifluoromethyl)aniline. Example **22** was obtained as a white solid (30 mg). LCMS ($M+H^+$): 338. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.31 (s, 1H), 8.34 (d, *J*=6.3 Hz, 2H), 7.83 (s, 1H), 7.56 - 7.42 (m, 4H), 7.33 - 7.21 (m, 2H), 4.95 (s, 2H), 4.23 (t, *J*=5.1 Hz, 2H), 4.11 - 3.98 (m, 2H).

Example 23:

N-(4-cyanophenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

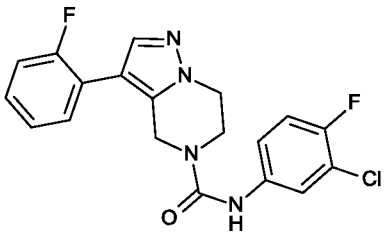


Preparation of Example 23:

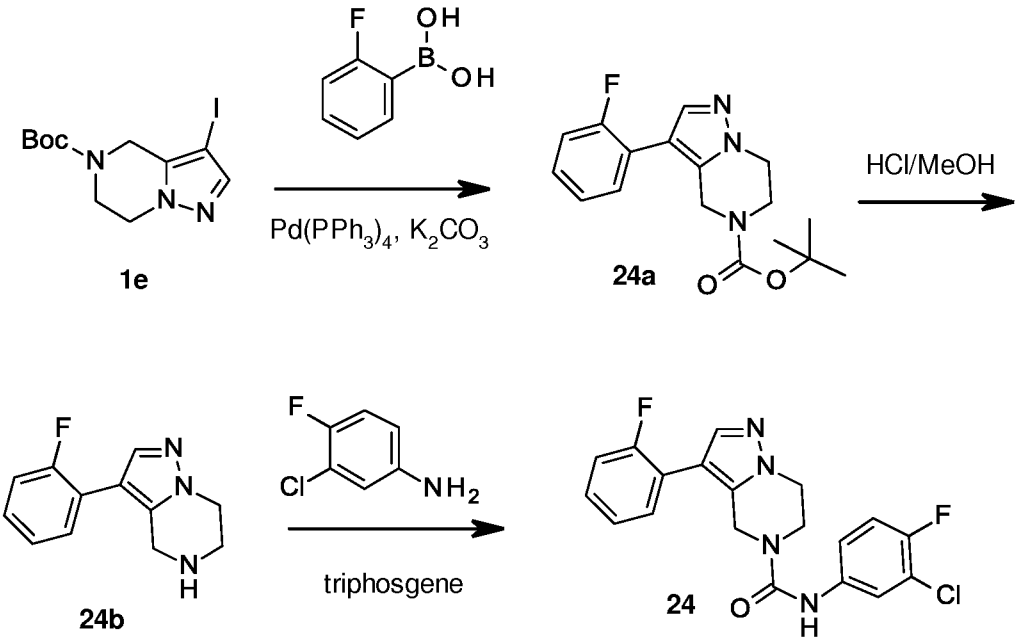
The title compound was prepared in analogy to the preparation of Example **11** by using 4-aminobenzonitrile instead of 3-(trifluoromethyl)aniline. Example **23** was obtained as a white solid (35 mg). LCMS ($M+H^+$): 362. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.35 (s, 1H), 7.83 (s, 1H), 7.75 - 7.63 (m, 4H), 7.49 (dd, *J*=5.5, 8.5 Hz, 2H), 7.27 (t, *J*=8.8 Hz, 2H), 4.95 (s, 2H), 4.24 (t, *J*=5.3 Hz, 2H), 4.02 (t, *J*=5.3 Hz, 2H).

Example 24:

N-(3-chloro-4-fluoro-phenyl)-3-(2-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of 3-(2-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound 24b):

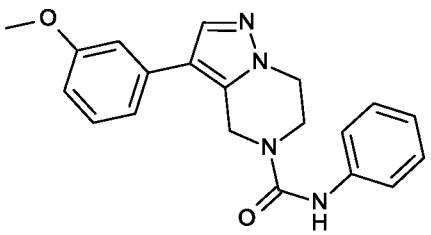
The compound **24b** was prepared in analogy to compound **11b** by using (2-fluorophenyl) boronic acid instead of (4-fluorophenyl)boronic acid. Compound **24b** was obtained as a white solid (250 mg). LCMS ($M+H^+$): 218.

Preparation of N-(3-chloro-4-fluoro-phenyl)-3-(2-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 24):

Example **24** was prepared in analogy to the preparation of Example **11** by using 3-choloro-4-fluoroaniline and 3-(2-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **24b**). Example **24** was obtained as a white solid (10 mg). LCMS ($M+H^+$): 389. ^1H NMR (400MHz, chloroform-d) ppm 7.77 (s, 1H), 7.50 (dd, *J*=2.6, 6.5 Hz, 1H), 7.39 - 7.31 (m, 2H), 7.27 - 7.16 (m, 3H), 7.12 - 7.04 (m, 1H), 6.57 (s, 1H), 4.79 (s, 2H), 4.40 (t, *J*=5.5 Hz, 2H), 4.07 (t, *J*=5.4 Hz, 2H).

Example 25:

3-(3-methoxyphenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

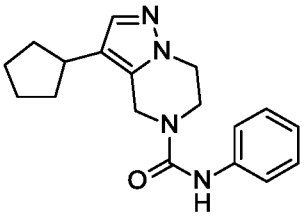


Preparation of Example 25:

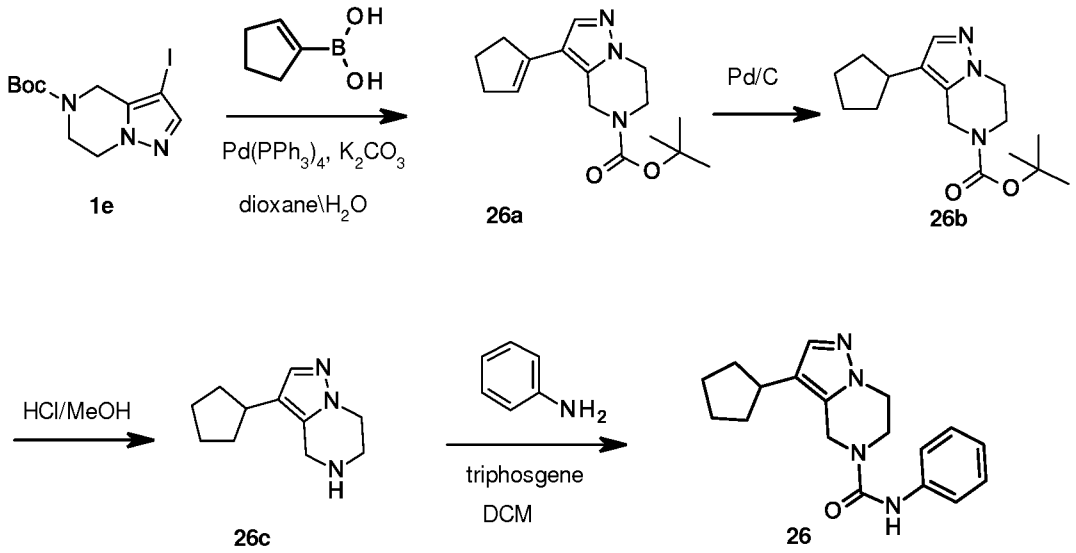
The title compound was prepared in analogy to the preparation of Example **1** by using (3-methoxylphenyl)boronic acid instead of (4-fluorophenyl)boronic acid. Example **25** was obtained as a white solid. LCMS ($M+H^+$): 349. ^1H NMR (400MHz, DMSO-d_6) ppm 8.91 (s, 1H), 7.86 (s, 1H), 7.44 (d, *J*=7.8 Hz, 2H), 7.35 (t, *J*=7.9 Hz, 1H), 7.25 (t, *J*=7.8 Hz, 2H), 7.07 - 6.94 (m, 3H), 6.85 (d, *J*=8.3 Hz, 1H), 4.95 (s, 2H), 4.22 (t, *J*=5.0 Hz, 2H), 4.01 (d, *J*=5.3 Hz, 2H), 3.81 (s, 3H).

Example 26:

3-cyclopentyl-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: **preparation of tert-butyl 3-(cyclopenten-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 26a)**

A mixture of cyclopenten-1-ylboronic acid (144 mg 1.2 mmol), Pd $(PPh_3)_4$ (240 mg, 0.03 mmol), Cs_2CO_3 (800 mg, 2.2 mmol) and tert-butyl 3-iodo-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **1e**, 400 mg, 1.1 mmol) in dioxane/H_2O (30 mL, 4:1, v/v) was refluxed for 12 hours under N_2. The reaction mixture was diluted with EtOAc (30 mL), washed with water (10 mL) and brine (10 mL). The organic layer was concentrated. The residue was purified by column chromatography to afford compound **26a** (275 mg) as a white solid. LCMS ($M+H^+$): 290.

Step 2: **preparation of tert-butyl 3-cyclopentyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 26b)**

To a solution of tert-butyl 3-(cyclopenten-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **26a**, 275 mg, 0.9 mmol) in MeOH (20 mL) was added Pd/C (80mg) under N_2, and the reaction mixture was stirred at room temperature for 12 hours under H_2. Then the solid was filtered off, the filtrate was concentrated to afford compound **26b** (270 mg) as a colorless oil. LCMS ($M+H^+$): 292.

Step 3: preparation of 3-cyclopentyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound 26c)

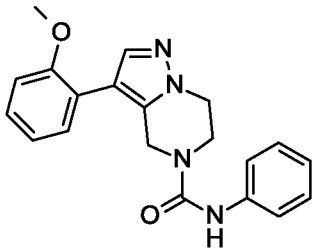
A solution of tert-butyl 3-cyclopentyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **26b**, 270 mg, 0.9 mmol) in HCl/MeOH (20 mL) was stirred at room temperature for 2 hours. Then the reaction mixture was concentrated in *vacuo* to afford compound **26c** (230 mg) as a slight yellow solid. LCMS ($M+H^+$): 192.

Step 4: preparation of 3-cyclopentyl-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 26)

The title compound was prepared in analogy to the preparation of Example **11** by using aniline and 3-cyclopentyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **26c**) instead of 3-(trifluoromethyl)aniline and 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine, respectively. Example **26** was obtained as a white solid. LCMS ($M+H^+$): 311. ^1H NMR (400 MHz, DMSO-d_6) δ ppm 8.81 (br. s, 1H), 7.46 (d, *J*=7.8 Hz, 2H), 7.35 - 7.19 (m, 3H), 6.98 (t, *J*=7.3 Hz, 1H), 4.69 (s, 2H), 4.15 - 4.04 (m, 2H), 3.93 (t, *J*=5.4 Hz, 2H), 2.88 - 2.76 (m, 1H), 2.26 - 1.21 (m, 8H).

Example 27:

3-(2-methoxyphenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

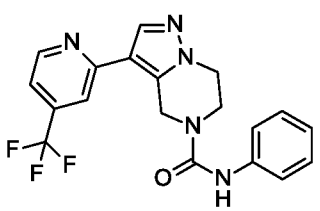


Preparation of Example 27:

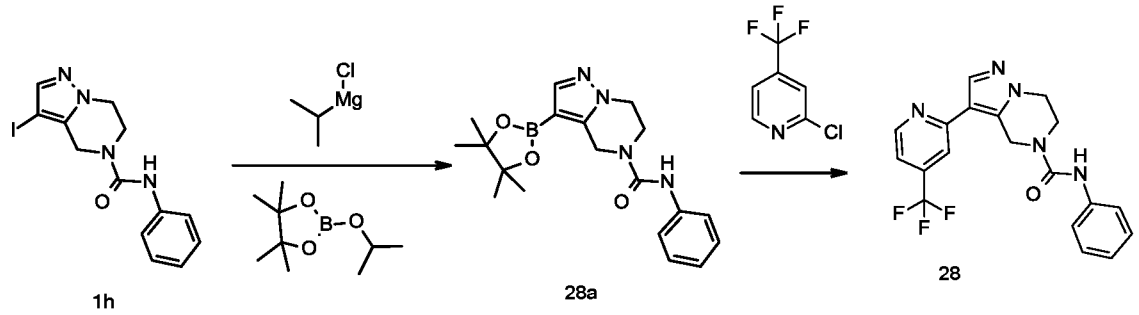
The title compound was prepared in analogy to the preparation of Example **1** by using (2-methoxylphenyl)boronic acid instead of (4-fluorophenyl)boronic acid. Example **27** was obtained as a white solid. LCMS ($M+H^+$): 349. ^1H NMR (400MHz, DMSO-d_6) δ ppm 8.84 (s, 1H), 7.63 - 7.61 (m, 1H), 7.43 (d, *J*=7.8 Hz, 2H), 7.34 - 7.21 (m, 4H), 7.09 (d, *J*=8.3 Hz, 1H), 6.98 (td, *J*=7.3, 19.0 Hz, 2H), 4.72 (s, 2H), 4.21 (t, *J*=5.3 Hz, 2H), 4.01 (t, *J*=5.4 Hz, 2H), 3.81 (s, 3H).

Example 28:

N-phenyl-3-[4-(trifluoromethyl)-2-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



Preparation of Example 28:



Step 1: **preparation of N-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (compound 28a)**

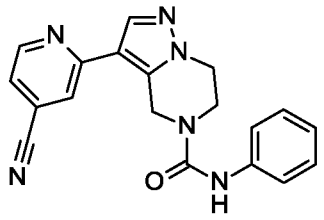
To a solution of 3-iodo-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (compound **1h**, 500 mg, 1.4 mmol) in THF (15 mL) was added isopropyl magnesium chloride (1.7 mL, 3.4 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 0.5 hours, then 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (380 mg, 2 mmol) in THF (5 mL) was added dropwise at 0 °C. The reaction mixture was stirred at room temperature for 1 hour. The reaction was quenched with saturated aqueous ammonium chloride solution (20 mL) slowly and extracted with EtOAc (30 mL). The organic layer was washed with brine, and concentrated to afford compound **28a** (450 mg) as a white solid. LCMS ($M+H^+$): 369.

Step 2: preparation of N-phenyl-3-[4-(trifluoromethyl)-2-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 28)

To a mixture of N-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (compound **28a**, 100 mg, 0.3 mmol), 2-chloro-4-(trifluoromethyl)pyridine (108 mg, 0.6 mmol) and K_2CO_3 (83 mg, 0.6 mmol) in DMSO/H_2O (10:1, 2 mL, v/v) was added Pd(dppf)Cl_2 (15 mg) under N_2. The resulting mixture was stirred at 80 °C for 12 hours. After cooled down, then the reaction mixture was filtered, and concentrated. The residue was purified by prep-HPLC to afford Example **28** (19 mg) as a white solid. LCMS ($M+H^+$): 388. ^1H NMR (400MHz, chloroform-d) δ ppm 8.77 (d, *J*=5.1 Hz, 1H), 8.06 (s, 1H), 7.73 (s, 1H), 7.42 - 7.33 (m, 5H), 7.16 - 7.11 (m, 1H), 6.79 (s, 1H), 5.18 (s, 2H), 4.39 (t, *J*=5.3 Hz, 2H), 4.10 (t, *J*=5.3 Hz, 2H).

Example 29:

3-(4-cyano-2-pyridyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

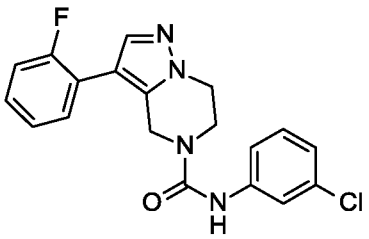


Preparation of Example 29:

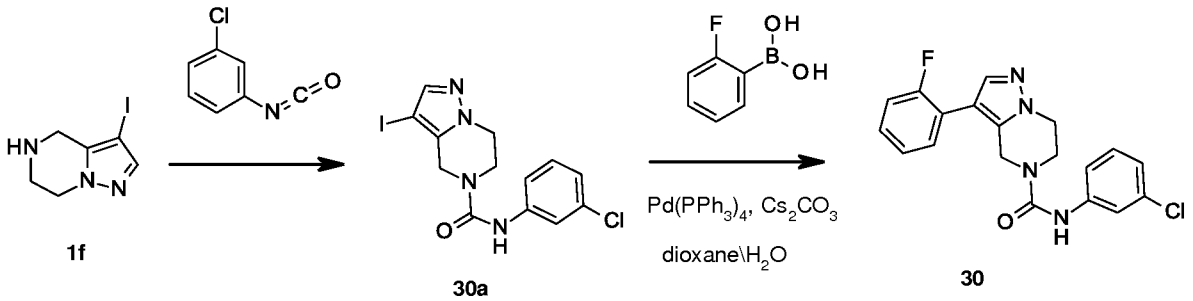
The title compound was prepared in analogy to the preparation of Example **28** by using 2-chloropyridine-4-carbonitrile instead of 2-chloro-4-(trifluoromethyl)pyridine. Example **29** was obtained as a white solid (11 mg). LCMS ($M+H^+$): 345. ^1H NMR (400MHz, DMSO-d6) δ ppm 8.75 (d, *J*=4.8 Hz, 1H), 7.98 (s, 1H), 7.74 (s, 1H), 7.42 - 7.32 (m, 5H), 7.31 - 7.12 (m, 1H), 6.65 (br. s, 1H), 5.14 (s, 2H), 4.37 (t, *J*=5.3 Hz, 2H), 4.09 (t, *J*=5.4 Hz, 2H).

Example 30:

N-(3-chlorophenyl)-3-(2-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



Preparation of Example 30:



Step 1: **preparation of N-(3-chlorophenyl)-3-iodo-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (compound 30a)**

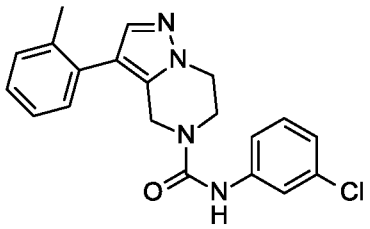
Compound **30a** was prepared in analogy to compound **1h** by using 1-chloro-3-isocyanato-benzene (500 mg) instead of isocyanatobenzene. Compound **30a** was obtained as a white solid (500 mg). LCMS ($M+H^+$): 403.

Step 2: preparation of N-(3-chlorophenyl)-3-(2-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 30)

To a solution of N-(3-chlorophenyl)-3-(2-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (compound **30a**, 0.1 g, 0.3 mmol) in dioxane/water (10 mL, 10:1, v/v) was added (2-fluorophenyl)boronic acid (40 mg, 0.33 mmol), $Pd(PPh_3)_4$ (10 mg, 0.09 mmol) and Cs_2CO_3 (195 mg, 0.6 mmol). The reaction mixture was stirred at 70 °C for 16 hours under nitrogen. The reaction mixture was concentrated and the residue was purified by prep-HPLC to afford Example **30** (5 mg) as a white solid. LCMS ($M+H^+$): 371. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.15 (br. s, 1H), 7.78 - 7.57 (m, 2H), 7.52 - 7.15 (m, 6H), 7.00 (d, *J*=7.3 Hz, 1H), 4.91 - 4.74 (m, 2H), 4.24 (br. s, 2H), 4.04 (br. s, 2H).

Example 31:

N-(3-chlorophenyl)-3-(o-tolyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

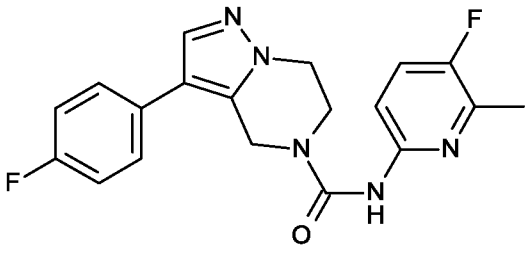


Preparation of Example 31:

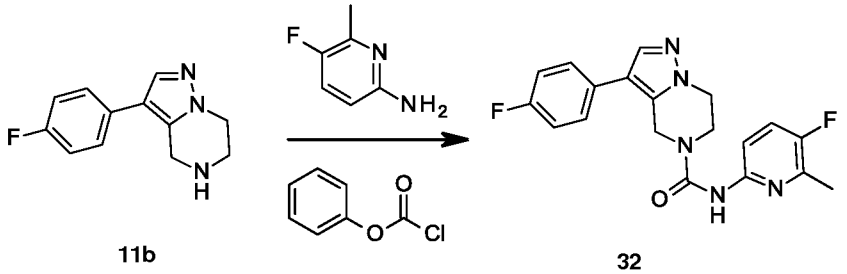
The title compound was prepared in analogy to the preparation of Example **30** by using (2-methylphenyl)boronic acid instead of (2-fluorophenyl)boronic acid. Example **31** was obtained as a white solid (10 mg). LCMS ($M+H^+$): 367. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.04 (s, 1H), 7.59 (d, *J*=12.8 Hz, 2H), 7.38 (d, *J*=8.0 Hz, 1H), 7.34 - 7.15 (m, 5H), 7.00 (d, *J*=7.9 Hz, 1H), 4.68 (s, 2H), 4.24 (br. s, 2H), 4.02 (br. s, 2H), 2.27 (s, 3H).

Example 32:

N-(5-fluoro-6-methyl-2-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



Preparation of Example 32:

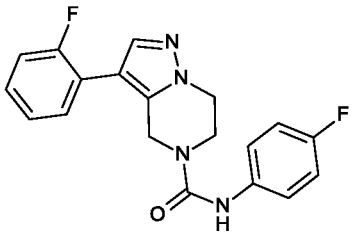


11b 32

To a mixture of 5-fluoro-6-methyl-pyridin-2-amine (40 mg, 0.32 mmol) and Et_3N (65 mg, 0.64 mmol) in THF (5 mL) was added phenyl chloroformate (50 mg, 0.12 mmol) slowly at 0 °C. The reaction mixture was stirred at room temperature for 12 hours. The reaction mixture was diluted with EtOAc (20 mL), washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (30 mL), and dried over anhydrous sodium sulfate. The solvents were removed in *vacuo*. The residue was dissolved in DMF (2 mL), to which 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**) (41 mg, 0.32 mmol) and DIPEA (0.2 mL) was added. Then the reaction mixture was stirred at 80 °C for 1 hour. The reaction mixture was subjected to prep-HPLC to afford Example **32** as a white solid. LCMS ($M+H^+$): 370. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.70 (s, 1H), 7.83 (s, 1H), 7.69 - 7.62 (m, 1H), 7.59 - 7.53 (m, 1H), 7.50 (dd, *J*=5.5, 8.7 Hz, 2H), 7.27 (t, *J*=8.8 Hz, 2H), 4.95 (s, 2H), 4.20 (t, *J*=5.3 Hz, 2H), 4.04 - 3.96 (m, 2H), 2.37 (d, *J*=2.8 Hz, 3H).

Example 33:

3-(2-fluorophenyl)-N-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

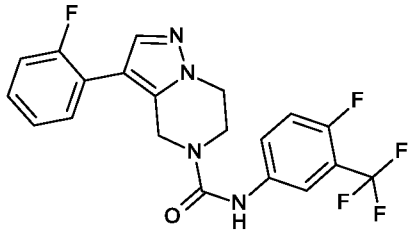


Preparation of Example 33:

The title compound was prepared in analogy to the preparation of Example **24** by using 4-fluoroaniline instead of 3-choloro-4-fluoroaniline. Example **33** was obtained as a white solid (45 mg). LCMS ($M+H^+$): 355. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.01 - 8.77 (m, 1H), 7.73 (d, *J*=1.9 Hz, 1H), 7.49 - 7.41 (m, 3H), 7.39 - 7.25 (m, 3H), 7.09 (t, *J*=8.9 Hz, 2H), 4.82 (s, 2H), 4.24 (t, *J*=5.4 Hz, 2H), 4.08 - 3.97 (m, 2H).

Example 34:

3-(2-fluorophenyl)-N-[4-fluoro-3-(trifluoromethyl)phenyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

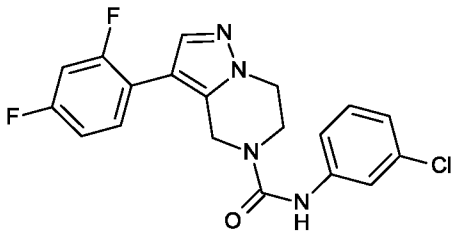


Preparation of Example 34:

The title compound was prepared in analogy to the preparation of Example **24** by using 3-trifluoro-4-fluoroaniline instead of 3-choloro-4-fluoroaniline. Example **34** was obtained as a white solid (21 mg). LCMS ($M+H^+$): 423. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.18 (s, 1H), 7.89 (dd, *J*=2.6, 6.3 Hz, 1H), 7.82 - 7.64 (m, 2H), 7.52 - 7.21 (m, 5H), 4.84 (s, 2H), 4.26 (t, *J*=5.4 Hz, 2H), 4.09 - 3.96 (m, 2H).

Example 35:

N-(3-chlorophenyl)-3-(2,4-difluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

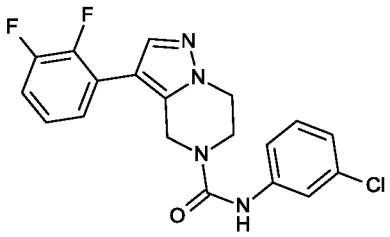


Preparation of Example 35:

The title compound was prepared in analogy to the preparation of Example **30** by using (3,4-difluorophenyl)boronic acid instead of (2-fluorophenyl)boronic acid. Example **35** was obtained as a white solid (15 mg). LCMS ($M+H^+$): 389. ^1H NMR (400MHz, chloroform-d) δ ppm 7.67 (s, 1H), 7.46 (s, 1H), 7.37 - 7.27 (m, 1H), 7.25 - 7.20 (m, 2H), 7.10 - 7.04 (m, 1H), 7.01 - 6.92 (m, 2H), 6.56 (s, 1H), 4.75 (s, 2H), 4.36 (t, *J*=5.5 Hz, 2H), 4.12 - 3.98 (m, 2H).

Example 36:

N-(3-chlorophenyl)-3-(2,3-difluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

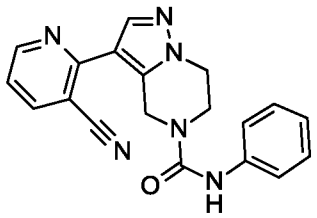


Preparation of Example 36:

The title compound was prepared in analogy to the preparation of Example **30** by using (3,4-difluorophenyl)boronic acid instead of (2-fluorophenyl)boronic acid. Example **36** was obtained as a white solid (23 mg). LCMS ($M+H^+$): 389. ^1H NMR (400MHz, chloroform-d) δ ppm 7.73 (s, 1H), 7.46 (d, J=1.3 Hz, 1H), 7.26 - 7.20 (m, 2H), 7.19 - 7.00 (m, 4H), 6.60 (s, 1H), 4.79 (s, 2H), 4.36 (t, J=5.5 Hz, 2H), 4.07 (t, J=5.5 Hz, 2H).

Example 37:

3-(3-cyano-2-pyridyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

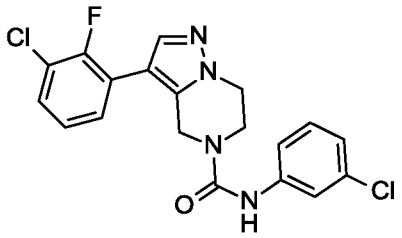


Preparation of Example 37:

The title compound was prepared in analogy to the preparation of Example **28** by using 2-chloropyridine-3-carbonitrile instead of 2-chloro-4-(trifluoromethyl)pyridine. Example **37** was obtained as a white solid (15 mg). LCMS ($M+H^+$): 345. ^1H NMR (400MHz, DMSO-d6) δ ppm 8.89 (s, 2H), 8.37 - 8.32 (m, 1H), 8.28 (s, 1H), 7.43 (s, 3H), 7.31 - 7.22 (m, 2H), 7.03 - 6.92 (m, 1H), 5.04 (s, 2H), 4.31 - 4.27 (m, 2H), 4.06 - 4.01 (m, 2H).

Example 38:

3-(3-chloro-2-fluoro-phenyl)-N-(3-chlorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

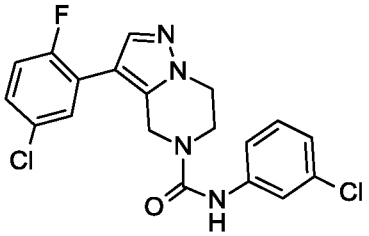


Preparation of Example 38:

The title compound was prepared in analogy to the preparation of Example **30** by using (2-fluoro-3-chlorophenyl)boronic acid instead of (2-fluorophenyl)boronic acid. Example **38** was obtained as a white solid (41 mg). LCMS ($M+H^+$): 405. ^1H NMR (400MHz, chloroform-d) δ ppm 7.76 (s, 1H), 7.47 - 7.37 (m, 2H), 7.28 - 7.21 (m, 3H), 7.20 - 7.15 (m, 1H), 7.10 - 7.05 (m, 1H), 6.64 (s, 1H), 4.79 (s, 2H), 4.41 (t, *J*=5.5 Hz,2H), 4.07 (t, *J*=5.5 Hz, 2H).

Example 39:

3-(5-chloro-2-fluoro-phenyl)-N-(3-chlorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

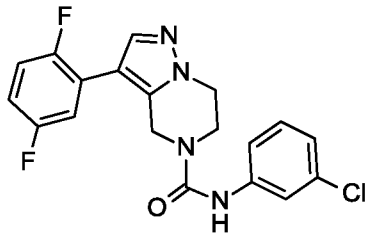


Preparation of Example 39:

The title compound was prepared in analogy to the preparation of Example **30** by using (2-fluoro-5-chlorophenyl)boronic acid instead of (2-fluorophenyl)boronic acid. Example **39** was obtained as a white solid (40 mg). LCMS ($M+H^+$): 405. ^1H NMR (400MHz, chloroform-d) δ ppm 7.71 (d, *J*=0.6 Hz, 1H), 7.46 (s, 1H), 7.33 (dd, *J*=2.6, 6.5 Hz, 1H), 7.30 - 7.25 (m, 1H), 7.25 - 7.22 (m, 2H), 7.13 (dd, *J*=8.8, 9.9 Hz, 1H), 7.09 - 7.04 (m, 1H), 6.59 (s, 1H), 4.78 (s, 2H), 4.36 (t, *J*=5.5 Hz, 2H), 4.06 (*t*, J=5.5 Hz, 2H).

Example 40:

N-(3-chlorophenyl)-3-(2,5-difluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

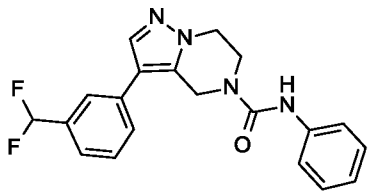


Preparation of Example 40:

The title compound was prepared in analogy to the preparation of Example **30** by using (2,5-difluorophenyl)boronic acid instead of (2-fluorophenyl)boronic acid. Example **40** was obtained as a white solid (23 mg). LCMS ($M+H^+$): 389. ^1H NMR (400MHz, chloroform-d) δ ppm 7.76 (s, 1H), 7.42 (s, 1H), 7.25 - 7.19 (m, 2H), 7.14 (dt, *J*=4.6, 9.3 Hz, 1H), 7.10 - 6.95 (m, 3H), 6.74 (s, 1H), 4.79 (s, 2H), 4.38 (t, *J*=5.4 Hz, 2H), 4.05 (t, *J*=5.5 Hz, 2H).

Example 41:

3-[3-(difluoromethyl)phenyl]-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

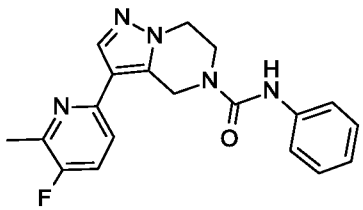


Preparation of Example 41:

The title compound was prepared in analogy to the preparation of Example **28** by using 1-bromo-3-(difluoromethyl)benzene instead of 2-chloro-4-(trifluoromethyl)pyridine. Example **41** was obtained as a white solid. LCMS ($M+H^+$): 369. ^1H NMR (400MHz, DMSO-d_6) δ ppm 8.91 (s, 1H), 7.90 (s, 1H), 7.67 - 7.54 (m, 3H), 7.49 - 7.39 (m, 3H), 7.25 (t, *J*=7.8 Hz, 2H), 7.05 - 6.97 (m, 2H), 4.96 (s, 2H), 4.22 (d, *J*=5.0 Hz, 2H), 4.01 (t, *J*=5.0 Hz, 2H).

Example 42:

3-(5-fluoro-6-methyl-2-pyridyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

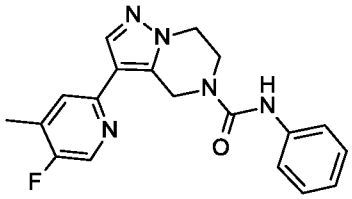


Preparation of Example 42:

The title compound was prepared in analogy to the preparation of Example **28** by using 6-chloro-3-fluoro-2-methyl-pyridine instead of 2-chloro-4-(trifluoromethyl)pyridine. Example **42** was obtained as a white solid. LCMS ($M+H^+$): 352. ^1H NMR (400MHz, DMSO-d_6) δ ppm 8.92 (s, 1H), 8.04 (s, 1H), 7.66 - 7.53 (m, 2H), 7.44 (d, *J*=8.0 Hz, 2H), 7.26 (t, *J*=7.8 Hz, 2H), 6.97 (t, *J*=7.3 Hz, 1H), 5.04 (s, 2H), 4.22 (t, *J*=4.9 Hz, 2H), 4.00 (t, *J*=5.1 Hz, 2H), 2.3 (s, 3H).

Example 43:

3-(5-fluoro-4-methyl-2-pyridyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

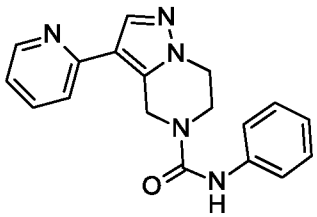


Preparation of Example 43:

The title compound was prepared in analogy to the preparation of Example **28** by using 2-chloro-5-fluoro-4-methyl-pyridine instead of 2-chloro-4-(trifluoromethyl)pyridine. Example **43** was obtained as a white solid. LCMS ($M+H^+$): 352. ^1H NMR (400MHz, DMSO-d_6) δ ppm 8.91 (s, 1H), 8.43 (s, 1H), 8.04 (s, 1H), 7.68 (d, *J*=6.0 Hz, 1H), 7.43 (d, *J*=7.8 Hz, 2H), 7.25 (t, *J*=7.8 Hz, 2H), 7.01 - 6.89 (m, 1H), 5.02 (s, 2H), 4.26 - 4.15 (m, 2H), 3.99 (t, *J*=5.0 Hz, 2H), 2.31 (s, 3H).

Example 44:

N-phenyl-3-(2-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



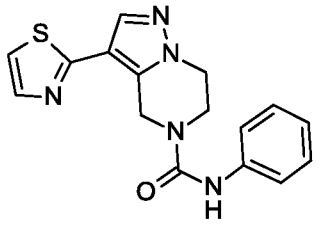
Preparation of Example 44:

The title compound was prepared in analogy to the preparation of Example **28** by using 2-chloropyridine instead of 2-chloro-4-(trifluoromethyl)pyridine. Example **44** was obtained as a white solid (30 mg). LCMS ($M+H^+$): 320. ^1H NMR (400MHz, methanol-d_4) δ ppm 8.68 (d, J=5.1 Hz, 1H), 8.30 (br. s, 1H), 8.15 (s, 1H), 7.91 (d, *J*=8.2 Hz, 1H), 7.63 (s, 1H), 7.43 - 7.39 (m,

2H), 7.33 - 7.28 (m, 2H), 7.09 - 7.05 (m, 1H), 5.15 (s, 2H), 4.37 (t, *J*=5.4 Hz, 2H), 4.13 (d, *J*=5.6 Hz, 2H).

Example 45:

N-phenyl-3-thiazol-2-yl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

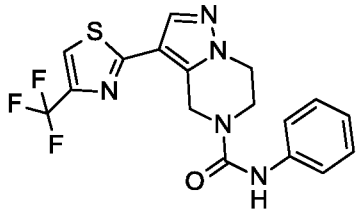


Preparation of Example 45:

The title compound was prepared in analogy to the preparation of Example **28** by using 2-bromothiazole instead of 2-chloro-4-(trifluoromethyl)pyridine. Example **45** was obtained as a white solid (12 mg). LCMS ($M+H^+$): 326. ^{1}H NMR (400MHz, methanol-d_4) δ ppm 8.01 (s, 1H), 7.84 (d, *J*=3.3 Hz, 1H), 7.53 (d, *J*=3.4 Hz, 1H), 7.44 - 7.40 (m, 2H), 7.30 (t, *J*=7.9 Hz, 2H), 7.10 - 7.03 (m, 1H), 5.11 (s, 2H), 4.35 - 4.31 (m, 2H), 4.10 (t, *J*=5.3 Hz, 2H).

Example 46:

N-phenyl-3-[4-(trifluoromethyl)thiazol-2-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

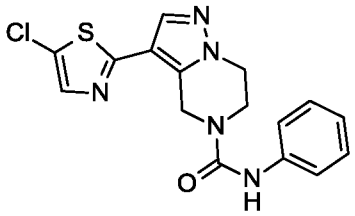


Preparation of Example 46:

The title compound was prepared in analogy to the preparation of Example **28** by using 4-trifluoromethy-2-bromothiazole instead of 2-chloro-4-(trifluoromethyl)pyridine. Example **46** was obtained as a white solid (12 mg). LCMS ($M+H^+$): 394. ^{1}H NMR (400MHz, methanol-d_4) δ ppm 8.06 (s, 2H), 7.42 - 7.38 (m, 2H), 7.34 - 7.24 (m, 2H), 7.11 - 7.02 (m, 1H), 5.12 (s, 2H), 4.37 - 4.32 (m, 2H), 4.10 (s, 2H).

Example 47:

3-(5-chlorothiazol-2-yl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

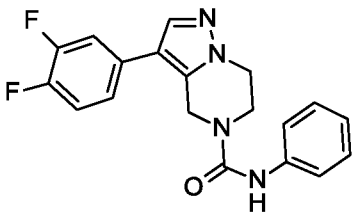


Preparation of Example 47:

The title compound was prepared in analogy to the preparation of Example **28** by using 5-chloro-2-bromothiazole instead of 2-chloro-4-(trifluoromethyl)pyridine. Example **47** was obtained as a white solid (17 mg). LCMS ($M+H^+$): 360. ^1H NMR (400MHz, methanol-d_4) δ ppm 7.95 (s, 1H), 7.67 (s, 1H), 7.44 - 7.39 (m, 2H), 7.34 - 7.25 (m, 2H), 7.10 - 7.02 (m, 1H), 5.07 (s, 2H), 4.37 - 4.27 (m, 2H), 4.10 - 4.06 (m, 2H).

Example 48:

3-(3,4-difluorophenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

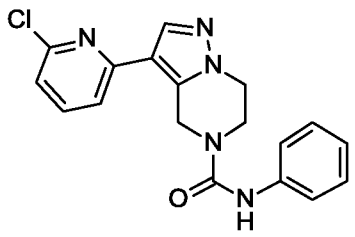


Preparation of Example 48:

The title compound was prepared in analogy to the preparation of Example **1** by using (3,4-difulorophenyl)boronic acid instead of (4-fluorophenyl)boronic acid. Example **48** was obtained as a white solid (10 mg). LCMS ($M+H^+$): 355. ^1H NMR (400MHz, DMSO-d_6) δ ppm 8.90 (s, 1H), 7.89 (s, 1H), 7.64 - 7.41 (m, 4H), 7.32 - 7.17 (m, 3H), 7.05 - 6.94 (m, 1H), 4.94 (s, 2H), 4.22 (t, *J*=5.3 Hz, 2H), 4.08 - 3.88 (m, 2H).

Example 49:

3-(6-chloro-2-pyridyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

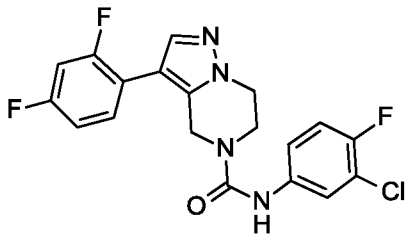


Preparation of Example 49:

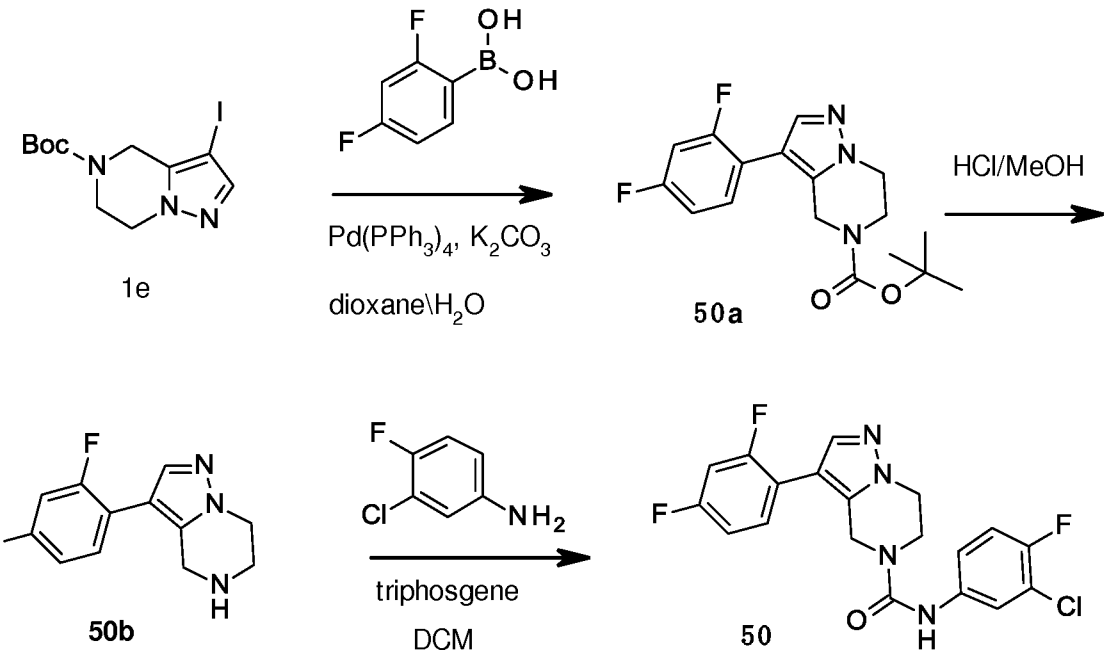
The title compound was prepared in analogy to the preparation of Example **28** by using 2,6-dichloropyridine instead of 2-chloro-4-(trifluoromethyl)pyridine. Example **49** was obtained as a white solid. LCMS ($M+H^+$): 354. ^1H NMR (400MHz, DMSO-d_6) δ ppm 8.92 (s, 1H), 8.14 (s, 1H), 7.88 - 7.83 (m, 1H), 7.69 (d, *J*=7.8 Hz, 1H), 7.46 (d, *J*=7.8 Hz, 2H), 7.31 - 7.22 (m, 3H), 7.00 - 6.95 (m, 1H), 5.04 (s, 2H), 4.25 (t, *J*=5.1 Hz, 2H), 4.02 (t, *J*=5.1 Hz, 2H).

Example 50:

N-(3-chloro-4-fluoro-phenyl)-3-(2,4-difluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of 3-(2,4-difluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (50b)

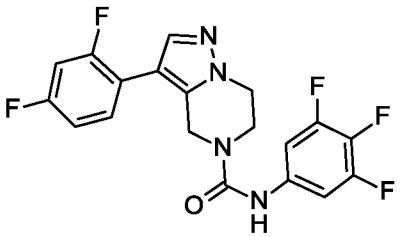
The compound **50b** was prepared in analogy to compound **11b** by using (2,4-difluorophenyl)boronic acid instead of (4-fluorophenyl)boronic acid. Compound **50b** was obtained as a white solid (250 mg). LCMS ($M+H^+$): 236.

Preparation of N-(3-chloro-4-fluoro-phenyl)-3-(2,4-difluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 50)

The title compound was prepared in analogy to the preparation of Example **11** by using 3-choloro-4-fluoroaniline instead of 3-trifluoromethyaniline and 3-(2,4-difluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **50b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **50** was obtained as a white solid (10 mg). LCMS ($M+H^+$): 407. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.15 (s, 1H), 7.80 - 7.61 (m, 2H), 7.59 - 7.24 (m, 4H), 7.24 - 7.12 (m, 1H), 4.79 (s, 2H), 4.24 (t, *J*=5.1 Hz, 2H), 4.07 - 3.93 (m, 2H).

Example 51:

3-(2,4-difluorophenyl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

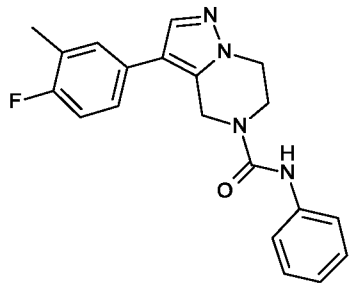


Preparation of Example 51:

The title compound was prepared in analogy to the preparation of Example **11** by using 3,4,5-trifluoroaniline instead of 3-trifluoromethylaniline and 3-(2,4-difluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **50b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **51** was obtained as a white solid (22 mg). LCMS ($M+H^+$): 409. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.31 (d, *J*=10.0 Hz, 1H), 7.70 (d, J=1.9 Hz, 1H), 7.55 - 7.29 (m, 4H), 7.19 (dt, *J*=2.4, 8.5 Hz, 1H), 4.80 (s, 2H), 4.24 (t, *J*=5.3 Hz, 2H), 4.12 - 3.93 (m, 2H).

Example 52:

3-(4-fluoro-3-methyl-phenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

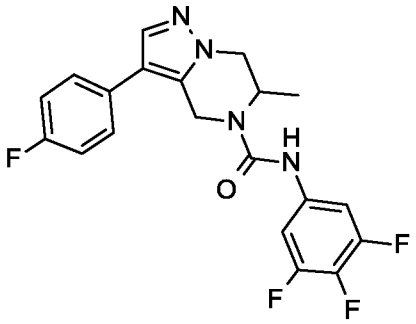


Preparation of Example 52:

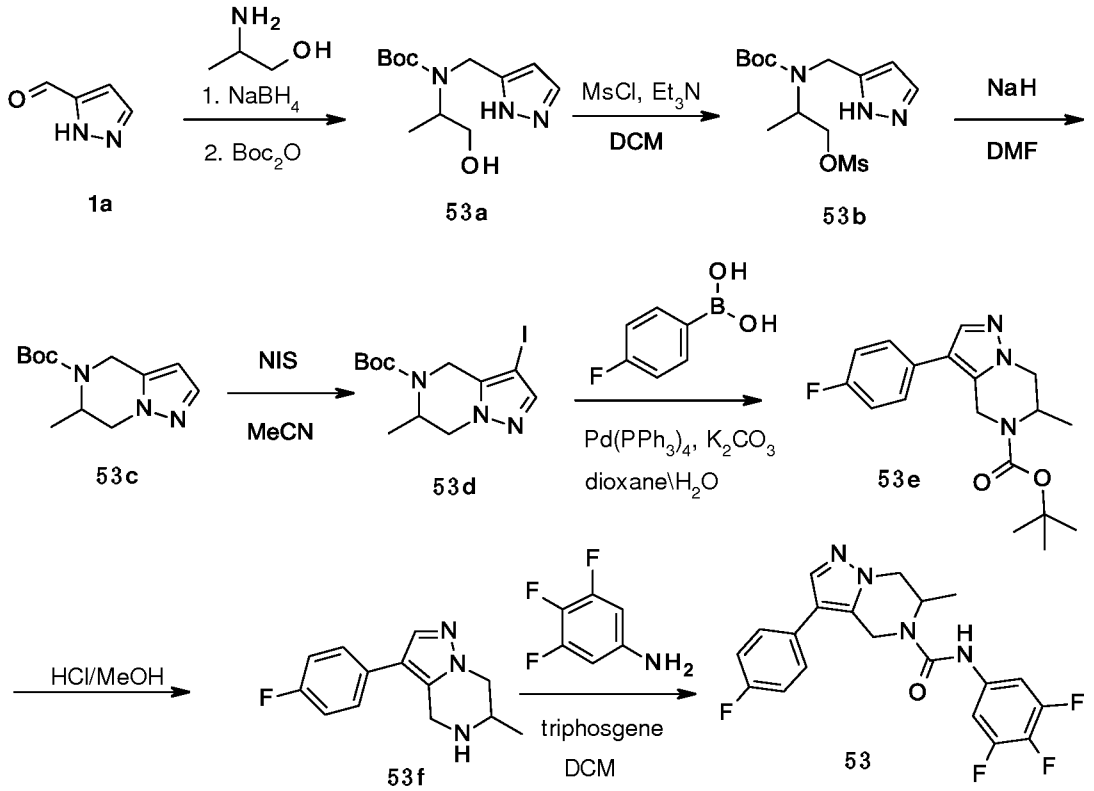
The title compound was prepared in analogy to the preparation of Example **1** by using (3-methyl-4-fluorophenyl)boronic acid instead of (4-fluorophenyl)boronic acid. Example **52** was obtained as a white solid (26 mg). LCMS ($M+H^+$): 351. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 8.89 (s, 1H), 7.80 (s, 1H), 7.45 (d, *J*=7.7 Hz, 2H), 7.40 - 7.35 (m, 1H), 7.31 - 7.12 (m, 4H), 7.03 - 6.91 (m, 1H), 4.92 (s, 2H), 4.22 (t, *J*=5.3 Hz, 2H), 4.07 - 3.92 (m, 2H), 2.29 (d, *J*=1.5 Hz, 3H).

Example 53:

3-(4-fluorophenyl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: preparation of tert-butyl N-(2-hydroxy-1-methyl-ethyl)-N-(1H-pyrazol-5-ylmethyl)carbamate (compound 53a)

To a solution of 1H-pyrazole-5-carbaldehyde (compound **1a**, 54.0 g, 562.5 mmol) in MeOH (300 mL) was added 2-aminopropan-1-ol (41.2 g, 675 mmol) and the reaction mixture was stirred at 25 °C for 1 hour. $NaBH_4$ (25.9 g, 675.0 mmol) was added at 0 °C and the reaction mixture was stirred for another 1 hour followed by the addition of H_2O (300 mL) and Boc_2O (147.1 g, 675.0 mmol). The resulting mixture was stirred at room temperature for 12 hours, and extracted with EtOAc (600 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography (eluting with 0%~5% MeOH in DCM) to afford compound **53a** (80 g) as a colorless oil. LCMS ($M+H^+$): 334. ^1H NMR (400MHz, chloroform-d) δ ppm 7.55 - 7.46 (m, 1H), 6.30 - 6.07 (m, 1H), 4.62 - 4.37 (m, 2H), 4.33 - 3.99 (m, 1H), 3.74 - 3.47 (m, 2H), 1.54 - 1.27 (m, 9H), 1.12 (d, J=7.0 Hz, 3H).

Step 2: preparation of 2-[tert-butoxycarbonyl(1H-pyrazol-5-ylmethyl)amino]propyl methanesulfonate (compound 53b)

To a mixture of tert-butyl N-(2-hydroxy-1-methyl-ethyl)-N-(1H-pyrazol-5-ylmethyl)carbamate (compound **53a**, 80.0 g, 117.2 mmol) and Et_3N (100.5 g, 995.6 mmol) in DCM (800 mL) was added MsCl (57.3 g, 497.8 mmol) slowly at 0 °C. The resulting mixture was stirred at room temperature for 2 hours, then washed with water (500 mL), brine (500 mL), and

dried over Na_2SO_4. The organic layer was concentrated to afford compound **53b** (100 g, crude), which was used directly in next step.

Step 3: preparation of tert-butyl 6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 53c)

To a solution of 2-[tert-butoxycarbonyl(1H-pyrazol-5-ylmethyl)amino]propyl methanesulfonate (compound **53b**, 100.0 g, 313.4 mmol) in DMF (1000 mL) was added NaH (15.0 g, 376.2 mmol) in portions at 0 °C. The reaction mixture was then stirred at room temperature for 12 hours, poured into water (2000 mL) and extracted with EtOAc (1000 mL) twice. The organic layers were combined and concentrated. The residue was purified by column chromatography (eluting with 10%~80% EtOAc in petroleum ether) to afford compound **53c** (18.0 g) as a colorless oil. LCMS ($M+H^+$): 238. ^1H NMR (400MHz, chloroform-d) δ ppm 7.55 - 7.46 (m, 1H), 6.20 (s, 1H), 4.98 - 4.91 (m, 1H), 4.85 - 4.76 (m, 1H), 4.45 - 4.33 (m, 1H), 4.26 - 4.18 (m, 1H), 4.16 - 4.08 (m, 1H), 1.53 (s, 9H), 1.23 - 1.10 (m, 3H).

Step 4: preparation of tert-butyl 3-iodo-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 53d)

To a solution of tert-butyl 6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **53c**, 3.3 g, 14.8 mmol) in CH_3CN (40 mL) was added NIS (5.0 g, 22.1 mmol) slowly. The reaction mixture was stirred at room temperature for 16 hours and then extracted with EtOAc (50 mL), washed with brine (50 mL). The organic layer was dried over Na_2SO_4 and concentrated, and the residue was purified by column chromatography (eluting with 10%~80% EtOAc in petroleum ether) to afford compound **53d** (4.8 g) as a white solid.

Step 5: **preparation of tert-butyl 3-(4-fluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 53e)**

To a mixture of tert-butyl 3-iodo-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **53d**, 1.1 g, 3 mmol), (4-fluorophenyl)boronic acid (630 mg, 4.5 mmol) and K_2CO_3 (1.2 g, 9 mmol) in and dioxane/water (10 mL, 5:1, v/v) was added $Pd(PPh_3)_4$ (150 mg) under N_2. The reaction mixture was stirred at 80 °C for 2 hours. The reaction was concentrated and the residue was purified by column chromatography to afford compound **53e** (550 mg) a slight yellow solid. LCMS ($M+H^+$): 332.

Step 6: preparation of 3-(4-fluorophenyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound 53f)

A solution of tert-butyl 3-(4-fluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **53e**, 550 mg, 1.7 mmol) in HCl/MeOH (20 mL) was stirred

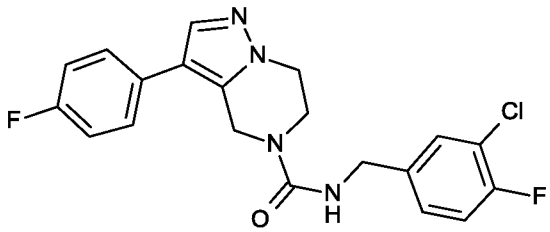
at room temperature for 2 hours. Then the reaction mixture was concentrated in *vacuo* to afford compound **53f** (400 mg) as a slight yellow solid. LCMS ($M+H^+$): 232.

Step 7: preparation of 3-(4-fluorophenyl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 53):

The title compound was prepared in analogy to the preparation of Example **11** by using 3,4,5-trifluoroaniline instead of 3-trifluoromethylaniline and 3-(4-fluorophenyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **53f**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **53** was obtained as a white solid (16 mg). LCMS ($M+H^+$): 405. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.12 (s, 1H), 7.86 (s, 1H), 7.55 (dd, *J*=5.4, 8.8 Hz, 2H), 7.43 (dd, *J*=6.5, 10.7 Hz, 2H), 7.27 (t, J=8.8 Hz, 2H), 5.19 (d, *J*=16.7 Hz, 1H), 4.95 - 4.87 (m, 1H), 4.66 (d, *J*=16.6 Hz, 1H), 4.28 - 4.17 (m, 1H), 3.54 (s, 1H), 1.18 (d, J=6.9 Hz, 3H).

Example 54:

N-[(3-chloro-4-fluoro-phenyl)methyl]-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

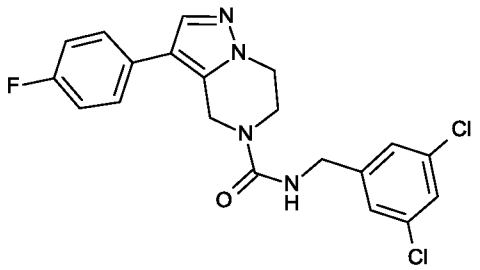


Preparation of Example 54:

The title compound was prepared in analogy to the preparation of Example **11** by using (3-chloro-4-fluoro-phenyl)methanamine instead of 3-(trifluoromethyl)aniline. Example **54** was obtained as a white solid (27 mg). LCMS ($M+H^+$): 403. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 7.81 (s, 1H), 7.55 (t, J=5.6 Hz, 1H), 7.50 - 7.46 (m, 3H), 7.35 - 7.25 (m, 4H), 4.81 (s, 2H), 4.25 (d, *J*=5.5 Hz, 2H), 4.14 (t, *J*=5.6 Hz, 2H), 3.89 (t, *J*=5.6 Hz, 2H).

Example 55:

N-[(3,5-dichlorophenyl)methyl]-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

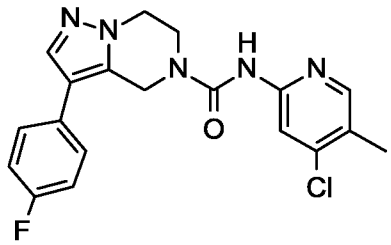


Preparation of Example 55:

The title compound was prepared in analogy to the preparation of Example **11** by using (3,5-dichloro-phenyl)methanamine instead of 3-(trifluoromethyl)aniline. Example **55** was obtained as a white solid. LCMS ($M+H^+$): 419. ^1H NMR (400MHz, DMSO-d_6) δ ppm 7.86 - 7.74 (m, 1H), 7.59 (t, J=5.7 Hz, 1H), 7.52 - 7.40 (m, 3H), 7.31 (d, *J*=1.9 Hz, 2H), 7.29 - 7.14 (m, 2H), 4.82 (s, 2H), 4.26 (d, *J*=5.8 Hz, 2H), 4.15 (t, *J*=5.3 Hz, 2H), 3.89 (t, *J*=5.3 Hz, 2H).

Example 56:

N-(4-chloro-5-methyl-2-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

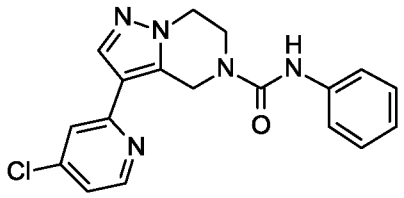


Preparation of Example 56:

The title compound was prepared in analogy to the preparation of Example **32** by using 4-chloro-5-methyl-pyridin-2-amine instead of 5-fluoro-6-methyl-pyridin-2-amine. Example **56** was obtaineded as a white solid (21 mg). LCMS ($M+H^+$): 386. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.85 (s, 1H), 8.21 (s, 1H), 7.91 (s, 1H), 7.83 (s, 1H), 7.50 (dd, *J*=5.5, 8.8 Hz, 2H), 7.34 - 7.19 (m, 2H), 4.96 (s, 2H), 4.25 - 4.16 (m, 2H), 4.05 - 3.97 (m, 2H), 2.25 (s, 3H).

Example 57:

3-(4-chloro-2-pyridyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

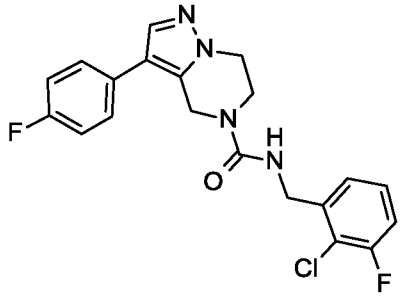


Preparation of Example 57:

The title compound was prepared in analogy to the preparation of Example **28** by using 2,4-dichloropyridine instead of 2-chloro-4-(trifluoromethyl)pyridine. Example **57** was obtained as a white solid. LCMS ($M+H^+$): 354. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.07 (s, 1H), 8.55 (d, *J*=5.5 Hz, 1H), 8.22 (s, 1H), 7.89 (d, *J*=1.8 Hz, 1H), 7.49 (d, *J*=7.8 Hz, 2H), 7.31 (dd, *J*=1.9, 5.4 Hz, 1H), 7.25 (t, *J*=7.9 Hz, 2H), 6.96 (t, *J*=7.4 Hz, 1H), 5.05 (s, 2H), 4.24 (t, *J*=5.1 Hz, 2H), 4.03 (t, *J*=5.1 Hz, 2H).

Example 58:

N-[(2-chloro-3-fluoro-phenyl)methyl]-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

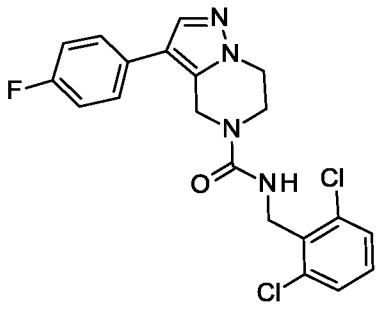


Preparation of Example 58:

The title compound was prepared in analogy to the preparation of Example **11** by using (2-chloro-3fluoro-phenyl)methanamine instead of 3-(trifluoromethyl)aniline. Example **58** was obtained as a white solid (26 mg). LCMS ($M+H^+$): 403. ^1H NMR (400MHz, DMSO-d_6) δ ppm 7.82 (s, 1H), 7.57 (t, *J*=5.5 Hz, 1H), 7.48 (dd, *J*=5.4, 8.7 Hz, 2H), 7.38 - 7.15 (m, 5H), 4.84 (s, 2H), 4.37 (d, *J*=5.5 Hz, 2H), 4.17 (t, *J*=5.1 Hz, 2H), 3.92 (d, *J*=5.3 Hz, 2H).

Example 59:

N-[(2,6-dichlorophenyl)methyl]-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

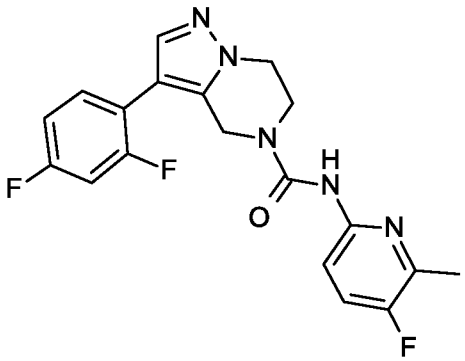


Preparation of Example 59:

The title compound was prepared in analogy to the preparation of Example **11** by using (2,5-dichloro-phenyl)methanamine instead of 3-(trifluoromethyl)aniline. Example **59** was obtained as a white solid (21 mg). LCMS ($M+H^+$): 419. ^1H NMR (400MHz, DMSO-d_6) δ ppm 7.78 (s, 1H), 7.53 - 7.41 (m, 4H), 7.39 - 7.31 (m, 1H), 7.28 - 7.17 (m, 2H), 7.09 (br. s, 1H), 4.76 (s, 2H), 4.49 (d, *J*=4.3 Hz, 2H), 4.10 (d, *J*=5.3 Hz, 2H), 3.87 (d, *J*=5.0 Hz, 2H).

Example 60:

3-(2,4-difluorophenyl)-N-(5-fluoro-6-methyl-2-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



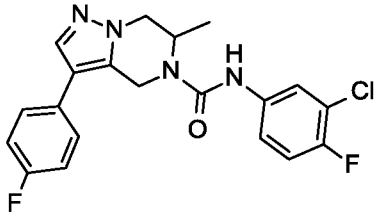
Preparation of Example 60:

To a mixture of 5-fluoro-6-methyl-pyridin-2-amine (40 mg, 0.32 mmol) and Et_3N (65 mg, 0.64 mmol) in THF (5 mL) was added phenyl chloroformate (50 mg, 0.12 mmol) at 0 °C. After stirred at room temperature for 12 hours, the reaction mixture was diluted with EtOAc (20 mL), washed with saturated aqueous $NaHCO_3$ (20 mL). The separated organic layer was washed with brine (30 mL), dried over anhydrous sodium sulfate. The solvent was removed in *vacuo*. The residue was dissolved in DMF (2 mL), to which were added 3-(2,4-difluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **50b**, 44 mg, 0.32 mmol) and DIPEA (0.2 mL). The resulting mixture was stirred at 80 °C for 1 hour, then subjected to purification by prep-HPLC to afford Example **60** (16 mg) as a white solid. LCMS ($M+H^+$): 388. ^1H NMR (400MHz,

DMSO-d_6) δ ppm 9.63 (br. s, 1H), 8.43 (br. s, 1H), 7.66 - 7.61 (m, 1H), 7.59 - 7.45 (m, 2H), 7.41 - 7.30 (m, 1H), 7.23 - 7.11 (m, 1H), 4.81 (s, 2H), 4.21 (d, J=5.0 Hz, 2H), 4.02 (s, 2H), 2.36 (d, J=2.5 Hz, 3H).

Example 61:

N-(3-chloro-4-fluoro-phenyl)-3-(4-fluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

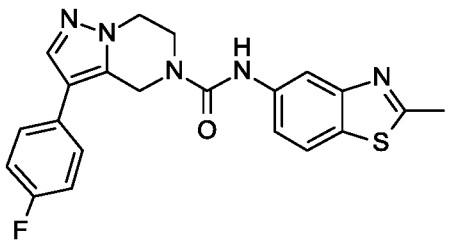


Preparation of Example 61:

The title compound was prepared in analogy to the preparation of Example **11** by using 3-chloro-4-fluoroaniline instead of 3-trifluoromethylaniline and 3-(4-fluorophenyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **53f**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **61** was obtained as a white solid (27 mg). LCMS ($M+H^+$): 403. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 8.96 (s, 1H), 7.86 (s, 1H), 7.74 (dd, *J*=2.5, 6.9 Hz, 1H), 7.55 (dd, *J*=5.5, 8.8 Hz, 2H), 7.45 - 7.40 (m, 1H), 7.36 - 7.30 (m, 1H), 7.27 (t, *J*=8.8 Hz, 2H), 5.20 (d, *J*=16.7 Hz, 1H), 4.96 - 4.87 (m, 1H), 4.65 (d, *J*=16.7 Hz, 1H), 4.29 - 4.22 (m, 1H), 4.21 - 4.14 (m, 1H), 1.18 (d, *J*=6.8 Hz, 3H).

Example 62:

3-(4-fluorophenyl)-N-(2-methyl-1,3-benzothiazol-5-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



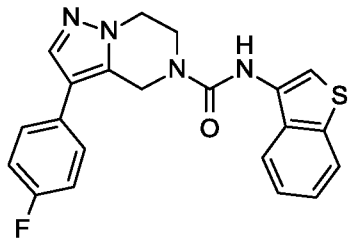
Preparation of Example 62:

The title compound was prepared in analogy to the preparation of Example **11** by using 2-methyl-1,3-benzothiazol-5-amine instead of 3-(trifluoromethyl)aniline. Example **62** was obtained as a white solid (33 mg). LCMS ($M+H^+$): 408. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.06 (s,

1H), 8.07 (d, *J*=1.8 Hz, 1H), 7.92 - 7.82 (m, 2H), 7.56 - 7.44 (m, 3H), 7.33 - 7.21 (m, 2H), 4.97 (s, 2H), 4.25 (t, *J*=5.3 Hz, 2H), 4.04 (t, *J*=5.1 Hz, 2H), 2.81 - 2.73 (m, 3H).

Example 63:

N-(benzothiophen-3-yl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

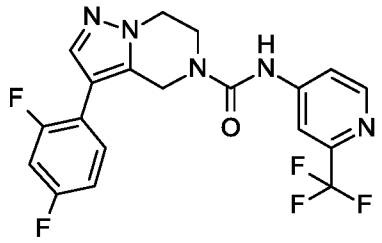


Preparation of Example 63:

The title compound was prepared in analogy to the preparation of Example **11** by using 2-methyl-1,3-benzothiazol-5-amine instead of 3-(trifluoromethyl)aniline. Example **63** was obtained as a white solid (24 mg). LCMS ($M+H^+$): 393. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.04 (s, 1H), 7.96 - 7.91 (m, 1H), 7.88 - 7.84 (m, 2H), 7.58 (s, 1H), 7.55 - 7.49 (m, 2H), 7.44 - 7.37 (m, 2H), 7.28 (t, *J*=8.8 Hz, 2H), 5.00 (s, 2H), 4.26 (t, *J*=5.2 Hz, 2H), 4.07 (t, *J*=5.4 Hz, 2H).

Example 64:

3-(2,4-difluorophenyl)-N-[2-(trifluoromethyl)-4-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



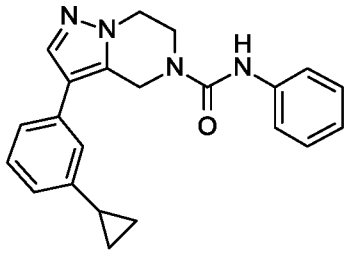
Preparation of Example 64:

The title compound was prepared in analogy to the preparation of Example **11** by using 2-(trifluoromethyl)pyridin-4-amine instead of 3-trifluoromethylaniline and 3-(2, 4-difluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **64** was afforded as a white solid (10 mg). LCMS ($M+H^+$): 424. ^1H NMR (400MHz, DMSO-d_6) δδ ppm 9.64 (s, 1H), 8.52 (d,

J=5.5 Hz, 1H), 8.00 (d, *J*=1.8 Hz, 1H), 7.72 (s, 2H), 7.55 - 7.46 (m, 1H), 7.44 - 7.35 (m, 1H), 7.20 (dt, *J*=2.4, 8.3 Hz, 1H), 4.84 (s, 2H), 4.27 (*t*, J=5.3 Hz, 2H), 4.06 (t, *J*=5.3 Hz, 2H).

Example 65:

3-(3-cyclopropylphenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

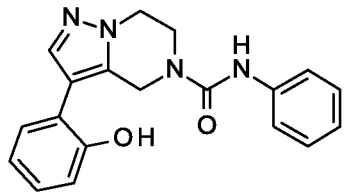


Preparation of Example 65:

The title compound was prepared in analogy to the preparation of Example **28** by using 1-bromo-3-cyclopropyl-benzene instead of 2-chloro-4-(trifluoromethyl)pyridine. Example **65** was obtained as a white solid (15 mg). LCMS ($M+H^+$): 359. ^1H NMR (400MHz, chloroform-d) δ ppm 7.76 (s, 1H), 7.39 - 7.31 (m, 5H), 7.10 (br. s, 3H), 7.03 - 6.96 (m, 1H), 6.70 - 6.53 (m, 1H), 4.90 (s, 2H), 4.38 (m, 2H), 4.04 (m, 2H), 2.00 - 1.90 (m, 1H), 1.11 - 0.98 (m, 2H), 0.81 - 0.68 (m, 2H).

Example 66:

3-(2-hydroxyphenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

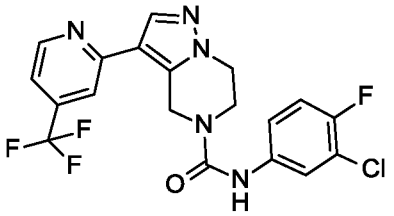


Preparation of Example 66:

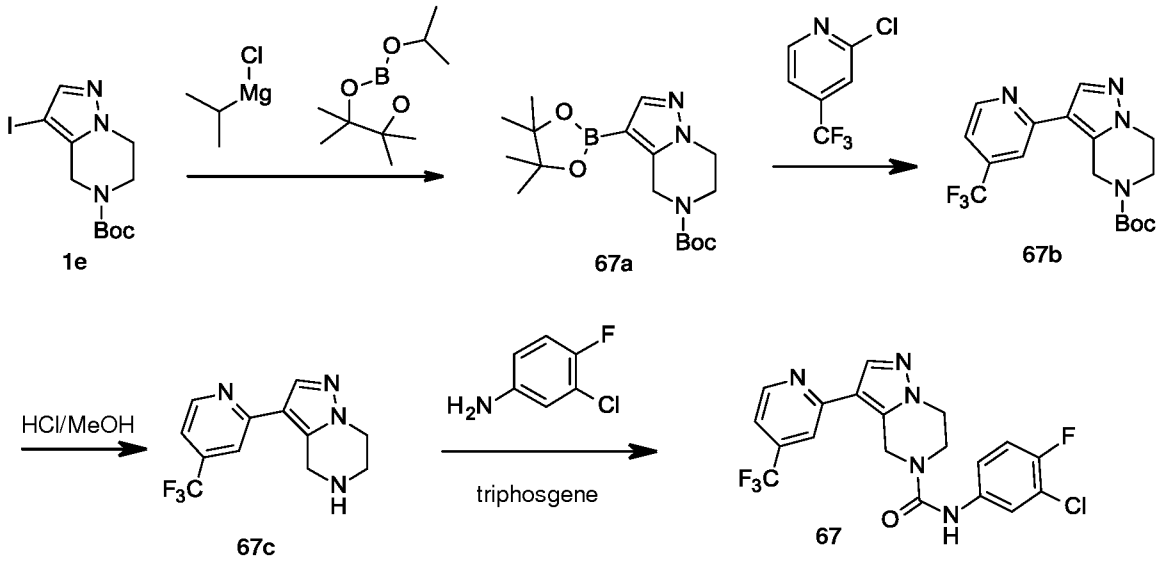
The title compound was prepared in analogy to the preparation of Example **28** by using 2-bromophenol instead of 2-chloro-4-(trifluoromethyl)pyridine. Example **66** was obtained as a white solid. LCMS ($M+H^+$): 335. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.65 (br. s, 1H), 8.84 (s, 1H), 7.64 (s, 1H), 7.43 (d, *J*=8.0 Hz, 2H), 7.27 - 7.17 (m, 3H), 7.12 (t, J=7.7 Hz, 1H), 6.99 - 6.90 (m, 2H), 6.85 (t, *J*=7.0 Hz, 1H), 4.76 (s, 2H), 4.21 (m, 2H), 4.00 (m, 2H).

Example 67:

N-(3-chloro-4-fluoro-phenyl)-3-[4-(trifluoromethyl)-2-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: **preparation of tert-butyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 67a)**

To a solution of tert-butyl 3-iodo-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **1e**, 500 mg, 1.4 mmol) in THF (15 mL) was added isopropyl magnesium chloride (1.7 mL, 3.4 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 0.5 hours, then 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (380 mg, 2 mmol) in THF (5 mL) was added dropwise at 0 °C. The reaction mixture was stirred at room temperature for 1 hour, then quenched with saturated aqueous ammonium chloride solution (20 mL), and extracted with EtOAc (30 mL). The organic layer was washed with brine, and concentrated to afford compound **67a** (450 mg) as a white solid. LCMS ($M+H^+$): 350.

Step 2: preparation of tert-butyl 3-[4-(trifluoromethyl)-2-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 67b)

To a mixture of tert-butyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **67a**, 450 mg, 1.3 mmol), 2-chloro-4-

(trifluoromethyl)pyridine (324 mg, 1.8 mmol) and K_2CO_3 (252 mg, 1.8 mmol) in DMSO/H_2O (10 mL, 10:1, v/v) was added Pd(dppf)Cl_2 (50 mg) under N_2. The reaction mixture was stirred at 80 °C for 12 hours. Then the reaction mixture was filtered, the filtrate was purified by column chromatography to afford compound **67b** (300 mg) as a white solid. LCMS ($M+H^+$): 369.

Step 3: preparation of 3-[4-(trifluoromethyl)-2-pyridyl]-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound 67c)

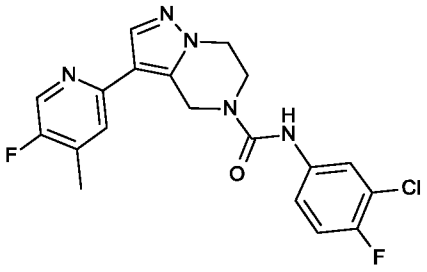
A solution of tert-butyl 3-[4-(trifluoromethyl)-2-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **67b**, 300 mg, 1.7 mmol) in HCl/MeOH (20 mL) was stirred at room temperature for 2 hours. Then the reaction mixture was concentrated in *vacuo* to afford compound **67c** (200 mg) as a slight yellow solid. LCMS ($M+H^+$): 269.

Step 4: Preparation of N-(3-chloro-4-fluoro-phenyl)-3-[4-(trifluoromethyl)-2-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 67)

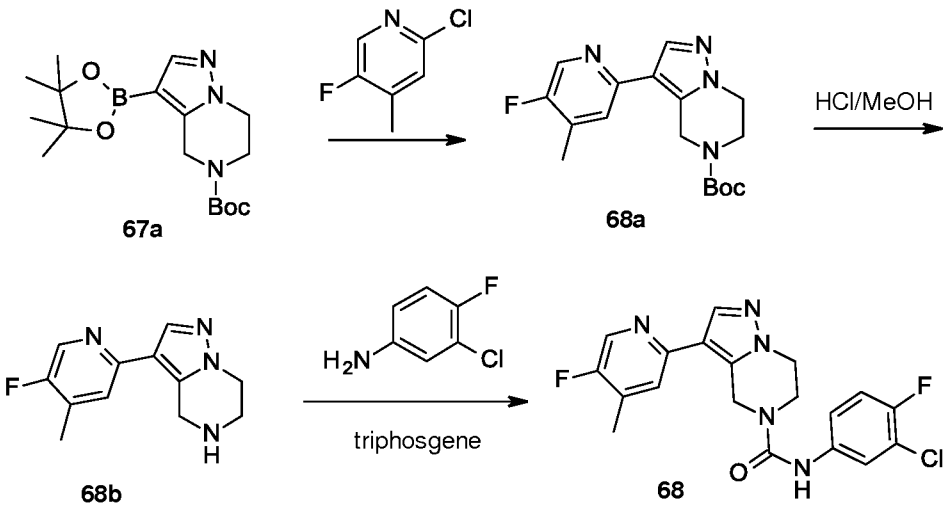
The title compound was prepared in analogy to the preparation of Example **11** by using 3-chloro-4-fluoroaniline and 3-[4-(trifluoromethyl)-2-pyridyl]-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **67c**) instead of 3-(trifluoromethyl)aniline and 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**), respectively. Example **67** was obtained as a white solid (8 mg). LCMS ($M+H^+$): 440. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.13 (br. s, 1H), 8.85 (d, *J*=5.0 Hz, 1H), 8.35 (s, 1H), 8.08 (br. s, 1H), 7.74 (d, *J*=4.4 Hz, 1H), 7.52 (d, *J*=4.3 Hz, 1H), 7.40 (br. s, 1H), 7.36 - 7.24 (m, 1H), 5.09 (s, 2H), 4.26 (m, 2H), 4.01 (m, 2H).

Example 68:

N-(3-chloro-4-fluoro-phenyl)-3-(5-fluoro-4-methyl-2-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



67a 68a 68b 68

Preparation of 3-(5-fluoro-4-methyl-2-pyridyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound 68b):

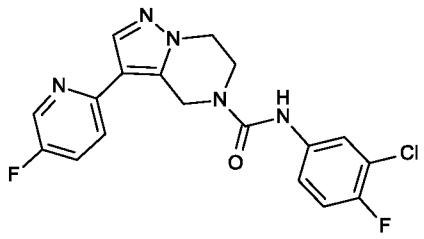
The compound **68b** was prepared in analogy to compound **67c** by using 2-chloro-5-fluoro-4-methyl-pyridine instead of 2-chloro-4-(trifluoromethyl)pyridine. Compound **68b** was obtained as a white solid (250 mg). LCMS ($M+H^+$): 233.

Preparation of N-(3-chloro-4-fluoro-phenyl)-3-(5-fluoro-4-methyl-2-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 68):

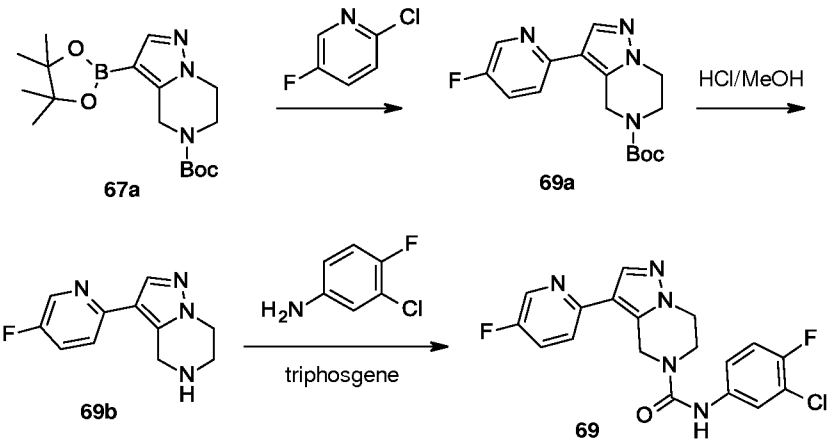
The title compound was prepared in analogy to the preparation of Example **11** by using 3-chloro-4-fluoroaniline and 3-(5-fluoro-4-methyl-2-pyridyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **68b**) instead of 3-(trifluoromethyl)aniline and 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**), respectively. Example **68** was obtained as a white solid (30 mg). LCMS ($M+H^+$): 404. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.09 (s, 1H), 8.45 (d, *J*=1.0 Hz, 1H), 8.06 (s, 1H), 7.78 - 7.67 (m, 2H), 7.45 - 7.39 (m, 1H), 7.35 - 7.29 (m, 1H), 5.03 (s, 2H), 4.23 (t, *J*=5.3 Hz, 2H), 3.99 (t, *J*=5.3 Hz, 2H), 2.32 (s, 3H).

Example 69:

N-(3-chloro-4-fluoro-phenyl)-3-(5-fluoro-2-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



67a 69a 69b 69

Preparation of 3-(5-fluoro-2-pyridyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound 69b):

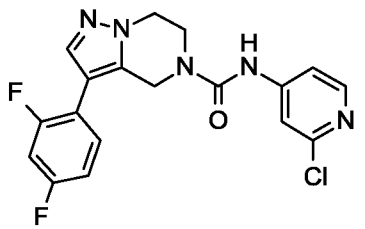
The compound **69b** was prepared in analogy to compound **67c** by using 2-chloro-5-fluoro-pyridine instead of 2-chloro-4-(trifluoromethyl)pyridine. Compound **69b** was obtained as a white solid (250 mg). LCMS ($M+H^+$): 219.

Preparation of N-(3-chloro-4-fluoro-phenyl)-3-(5-fluoro-2-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 69):

The title compound was prepared in analogy to the preparation of Example **11** by using 3-chloro-4-fluoroaniline instead of 3-(trifluoromethyl)aniline and 3-(5-fluoro-2-pyridyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **69b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **69** was obtained as a white solid (50 mg). LCMS ($M+H^+$): 390. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.09 (s, 1H), 8.58 (d, *J*=2.5 Hz, 1H), 8.10 (s, 1H), 7.78 (s, 3H), 7.45 - 7.39 (m, 1H), 7.36 - 7.29 (m, 1H), 5.04 (s, 2H), 4.24 (t, *J*=5.3 Hz, 2H), 4.00 (t, *J*=5.3 Hz, 2H).

Example 70:

N-(2-chloro-4-pyridyl)-3-(2,4-difluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

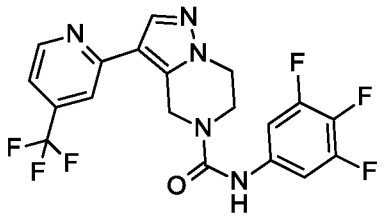


Preparation of Example 70:

The title compound was prepared in analogy to the preparation of Example **11** by using 2-chloropyridin-4-amine instead of 3-trifuloromethylaniline and 3-(2,4-difluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **70** was obtained as a white solid (27 mg). LCMS ($M+H^+$): 390. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.49 (s, 1H), 8.16 (d, *J*=5.8 Hz, 1H), 7.71 (d, *J*=1.3 Hz, 1H), 7.61 (d, *J*=1.3 Hz, 1H), 7.55 - 7.30 (m, 3H), 7.25 - 7.13 (m, 1H), 4.82 (s, 2H), 4.26 (t, *J*=5.3 Hz, 2H), 4.10 - 3.98 (m, 2H).

Example 71:

3-[4-(trifluoromethyl)-2-pyridyl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

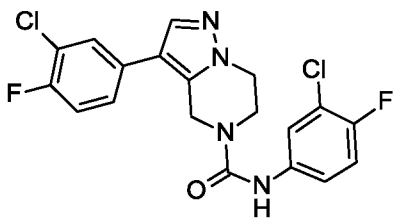


Preparation of Example 71:

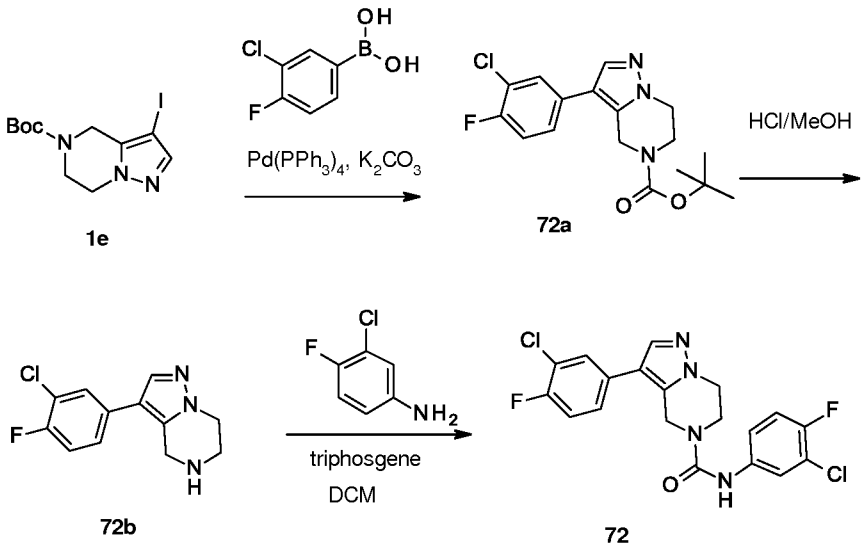
The title compound was prepared in analogy to Example **11** by using 3,4,5-trifluoroaniline instead of 3-(trifluoromethyl)aniline and 3-[4-(trifluoromethyl)-2-pyridyl]-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **67c**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **71** was obtained as a white solid. LCMS ($M+H^+$): 442. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.35 (s, 1H), 8.85 (d, *J*=5.1 Hz, 1H), 8.35 (s, 1H), 8.09 (s, 1H), 7.52 (d, *J*=5.0 Hz, 1H), 7.43 (dd, *J*=6.4, 10.7 Hz, 2H), 5.09 (s, 2H), 4.26 (d, *J*=5.3 Hz, 2H), 4.03 (d, *J*=5.4 Hz, 2H).

Example 72:

N,3-bis(3-chloro-4-fluoro-phenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of 3-(3-chloro-4-fluoro-phenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound 72b):

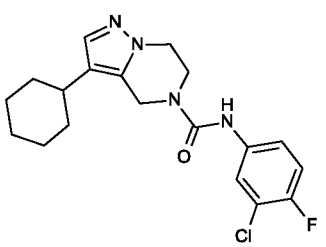
The compound **72b** was prepared in analogy to compound **11b** by using (3-chloro-4-fluoro-phenyl)boronic acid (300 mg) instead of (4-fluoro-phenyl)boronic acid. Compound **72b** was obtained as a white solid (250 mg). LCMS ($M+H^+$): 252.

Preparation of N,3-bis(3-chloro-4-fluoro-phenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 72):

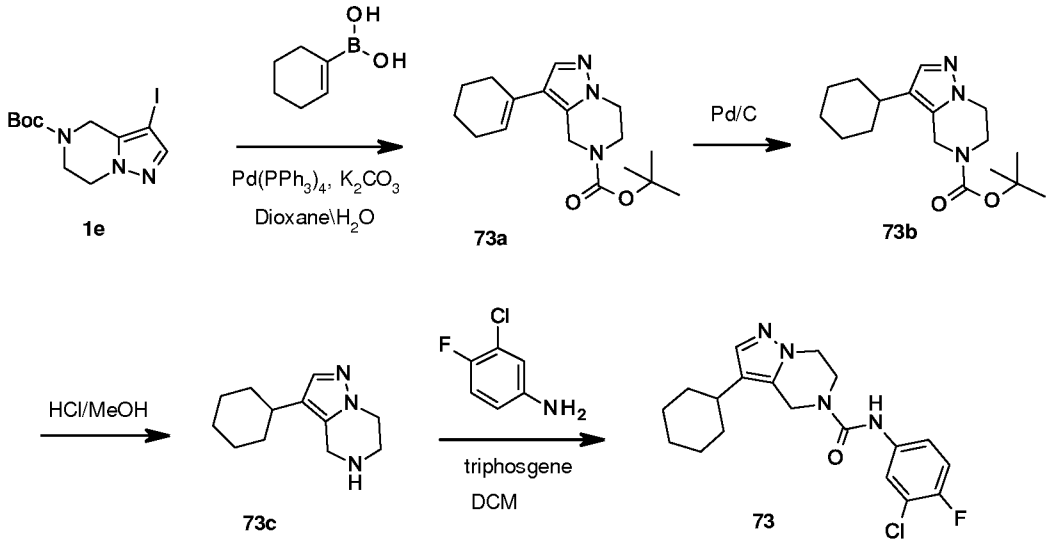
The title compound was prepared in analogy to the preparation of Example **11** by using 3-chloro-4-fluoroaniline instead of 3-(trifluoromethyl)aniline and 3-(3-chloro-4-fluoro-phenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **72b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **72** was obtained as a white solid (10 mg). LCMS ($M+H^+$): 443. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.09 (s, 1H), 7.90 (s, 1H), 7.76 - 7.61 (m, 2H), 7.55 - 7.37 (m, 3H), 7.37 - 7.27 (m, 1H), 4.95 (s, 2H), 4.22 (d, *J*=4.8 Hz, 2H), 3.99 (m, 2H).

Example 73:

N-(3-chloro-4-fluoro-phenyl)-3-cyclohexyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of 3-cyclohexyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound 73c):

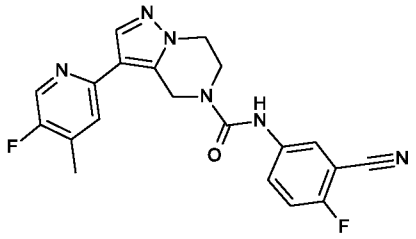
The compound **73c** was prepared in analogy to compound **26c** by using cyclohexen-1-ylboronic acid instead of cyclopenten-1-ylboronic acid. Compound **73c** was obtained as a white solid (250 mg). LCMS ($M+H^+$): 306.

Preparation of N-(3-chloro-4-fluoro-phenyl)-3-cyclohexyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 73):

The title compound was prepared in analogy to the preparation of Example **11** by using 3-chloro-4-fluoroaniline instead of 3-(trifluoromethyl)aniline and 3-cyclohexyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **73c**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **73** was obtained as a white solid (10 mg). LCMS ($M+H^+$): 377. ^1H NMR (400MHz, DMSO-d_6) δ ppm 8.98 (s, 1H), 7.75 (dd, *J*=2.5, 6.8 Hz, 1H), 7.44 (td, *J*=4.3, 7.2 Hz, 1H), 7.36 - 7.32 (m, 1H), 7.31 - 7.29 (m, 1H), 4.69 (s, 2H), 4.13 - 4.08 (m, 2H), 3.95 - 3.90 (m, 2H), 2.42 (m, 1H), 1.86 - 1.63 (m, 5H), 1.38 - 1.20 (m, 5H).

Example 74:

N-(3-cyano-4-fluoro-phenyl)-3-(5-fluoro-4-methyl-2-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

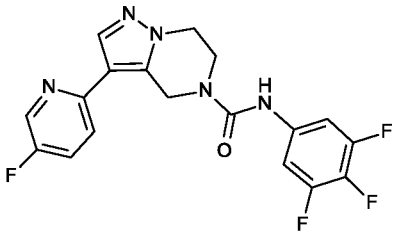


Preparation of Example 74:

The title compound was prepared in analogy to the preparation of Example **11** by using 5-amino-2-fluoro-benzonitrile instead of 3-(trifluoromethyl)aniline and 3-(5-fluoro-4-methyl-2-pyridyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **68b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **74** was obtained as a white solid (16 mg). LCMS ($M+H^+$): 396. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.25 (s, 1H), 8.45 (s, 1H), 8.06 (s, 1H), 7.95 (d, *J*=2.8 Hz, 1H), 7.82 - 7.76 (m, 1H), 7.71 (d, *J*=6.0 Hz, 1H), 7.51 - 7.43 (m, 1H), 5.05 (s, 2H), 4.24 (t, *J*=5.2 Hz, 2H), 4.03 - 3.99 (m, 2H), 2.32 (s, 3H).

Example 75:

3-(5-fluoro-2-pyridyl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

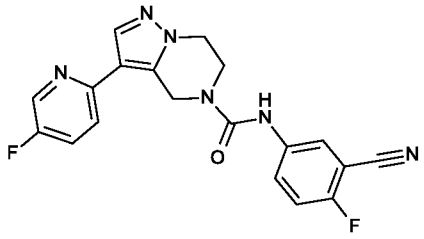


Preparation of Example 75:

The title compound was prepared in analogy to the preparation of Example **11** by using 3,4,5-trifluoroaniline instead of 3-(trifluoromethyl)aniline and 3-(5-fluoro-2-pyridyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **69b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **75** was obtained as a white solid (50 mg). LCMS ($M+H^+$): 392. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.35 - 9.22 (m, 1H), 8.58 (d, *J*=2.6 Hz, 1H), 8.11 (s, 1H), 7.82 - 7.68 (m, 2H), 7.51 - 7.36 (m, 2H), 5.05 (s, 2H), 4.24 (t, *J*=5.3 Hz, 2H), 4.01 (t, *J*=5.0 Hz, 2H).

Example 76:

N-(3-cyano-4-fluoro-phenyl)-3-(5-fluoro-2-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

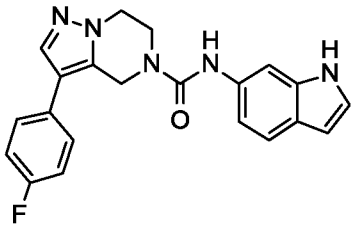


Preparation of Example 76:

The title compound was prepared in analogy to the preparation of Example **11** by using 5-amino-2-fluoro-benzonitrile instead of 3-(trifluoromethyl)aniline and 3-(5-fluoro-2-pyridyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **69b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **76** was obtained as a white solid (42 mg). LCMS ($M+H^+$): 381. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.26 (s, 1H), 8.58 (d, *J*=2.5 Hz, 1H), 8.11 (s, 1H), 7.94 (dd, *J*=2.6, 5.8 Hz, 1H), 7.83 - 7.71 (m, 3H), 7.46 (t, *J*=9.2 Hz, 1H), 5.06 (s, 2H), 4.25 (t, *J*=5.3 Hz, 2H), 4.01 (t, *J*=5.3 Hz, 2H).

Example 77:

3-(4-fluorophenyl)-N-(1H-indol-6-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

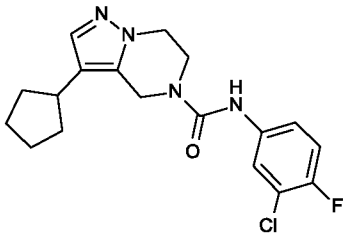


Preparation of Example 77:

The title compound was prepared in analogy to the preparation of Example **11** by using 1H-indol-6-amine instead of 3-(trifluoromethyl)aniline. Example **77** was obtained as a white solid (17 mg). LCMS ($M+H^+$):376. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 10.92 (s, 1H), 8.78 (s, 1H), 7.83 (s, 1H), 7.60 (s, 1H), 7.55 - 7.47 (m, 2H), 7.39 (d, *J*=8.5 Hz, 1H), 7.31 - 7.18 (m, 3H), 7.00 (d, *J*=8.3 Hz, 1H), 6.33 (s, 1H), 4.96 - 4.93 (m, 2H), 4.25- 4.21 (m, 2H), 4.03-4.00 (m, 2H).

Example 78:

N-(3-chloro-4-fluoro-phenyl)-3-cyclopentyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

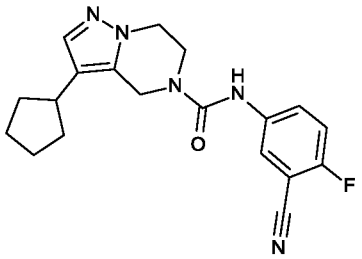


Preparation of Example 78:

The title compound was prepared in analogy to the preparation of Example **11** by using 3-chloro-4-fluoroaniline instead of 3-(trifluoromethyl)aniline and 3-cyclopentyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **26c**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **78** was obtained as a white solid. LCMS ($M+H^+$): 363. ^1H NMR (400 MHz, DMSO-d_6) δ ppm 9.00 (s, 1H), 7.76 (dd, *J*=2.5, 6.8 Hz, 1H), 7.47 - 7.43 (m, 1H), 7.38 - 7.27 (m, 2H), 4.69 (s, 2H), 4.15 - 4.05 (m, 2H), 3.93 (t, *J*=5.3 Hz, 2H), 2.88 - 2.76 (m, 1H), 2.02 - 1.89 (m, 2H), 1.78 - 1.55 (m, 4H), 1.49 - 1.39 (m, 2H).

Example 79:

N-(3-cyano-4-fluoro-phenyl)-3-cyclopentyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

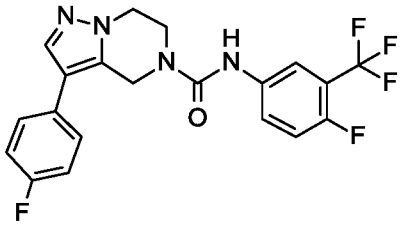


Preparation of Example 79:

The title compound was prepared in analogy to the preparation of Example **11** by using 5-amino-2-fluorobenzonitrile instead of 3-(trifluoromethyl)aniline and 3-cyclopentyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **26c**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **79** was obtained as a white solid. LCMS ($M+H^+$): 354. ^1H NMR (400 MHz, DMSO-d_6) δ ppm 7.76 - 7.72 (m, 1H), 7.63 (dd, *J*=2.8, 5.3 Hz, 1H), 7.49 (s, 1H), 7.37 (s, 1H), 7.16 (t, *J*=8.8 Hz, 1H), 4.74 (s, 2H), 4.23 (t, J=5.3 Hz, 2H), 3.98 (t, J=5.3 Hz, 2H), 2.88 - 2.73 (m, 1H), 2.06 - 1.98 (m, 2H), 1.82 - 1.60 (m, 4H), 1.56 - 1.44 (m, 2H).

Example 80:

3-(4-fluorophenyl)-N-[4-fluoro-3-(trifluoromethyl)phenyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

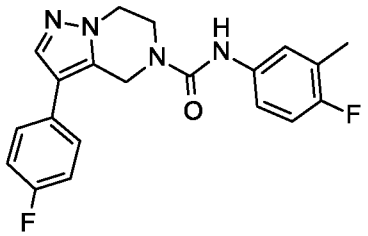


Preparation of Example 80:

The title compound was prepared in analogy to the preparation of Example **11** by using 4-fluoro-3-trifluoromethylaniline instead of 3-(trifluoromethyl)aniline. Example **80** was obtained as a white solid (17 mg). LCMS ($M+H^+$): 423. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.21 (s, 1H), 7.98 - 7.71 (m, 3H), 7.57 - 7.37 (m, 3H), 7.27 (t, *J*=8.8 Hz, 2H), 4.94 (s, 2H), 4.23 (d, *J*=4.8 Hz, 2H), 4.02 (d, *J*=5.0 Hz, 2H).

Example 81:

N-(4-fluoro-3-methyl-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

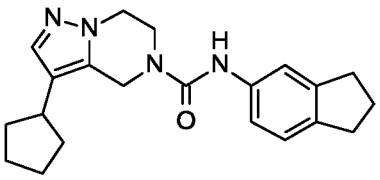


Preparation of Example 81:

The title compound was prepared in analogy to the preparation of Example **11** by using 4-fluoro-3-methyl-aniline instead of 3-(trifluoromethyl)aniline. Example **81** was obtained as a white solid (36 mg). LCMS ($M+H^+$): 369. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 8.86 (s, 1H), 7.82 (s, 1H), 7.49 (dd, *J*=5.6, 8.4 Hz, 2H), 7.38 - 7.22 (m, 4H), 7.02 (t, *J*=9.2 Hz, 1H), 4.91 (s, 2H), 4.21 (t, *J*=5.1 Hz, 2H), 3.99 (t, *J*=5.0 Hz, 2H), 2.19 (s, 3H).

Example 82:

3-cyclopentyl-N-indan-5-yl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

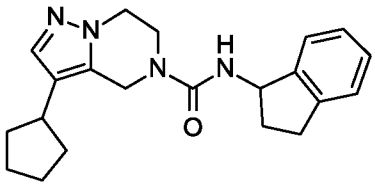


Preparation of Example 82:

The title compound was prepared in analogy to the preparation of Example **11** by using indan-5-amine instead of 3-(trifluoromethyl)aniline and 3-cyclopentyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **26c**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **82** was obtained as a white solid. LCMS ($M+H^+$): 351. ^1H NMR (400 MHz, chloroform-d) δ ppm 7.50 (s, 1H), 7.30 - 7.24 (m, 1H), 7.16 (d, *J*=8.0 Hz, 1H), 7.04 (d, *J*=7.5 Hz, 1H), 6.81 (br. s, 1H), 4.72 (s, 2H), 4.43 - 4.17 (m, 2H), 3.96 (s, 2H), 2.94 - 2.76 (m, 5H), 2.15 - 1.98 (m, 4H), 1.87 - 1.62 (m, 4H), 1.57 - 1.44 (m, 2H).

Example 83:

3-cyclopentyl-N-indan-1-yl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

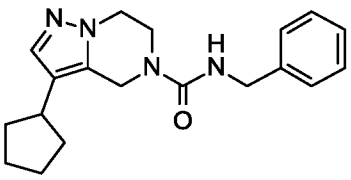


Preparation of Example 83:

The title compound was prepared in analogy to the preparation of Example **11** by using indan-1-amine instead of 3-(trifluoromethyl)aniline and 3-cyclopentyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **26c**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **83** was obtained as a white solid. LCMS ($M+H^+$): 351. ^1H NMR (400 MHz, chloroform-d) δ ppm 7.49 (s, 1H), 7.36 (d, *J*=6.8 Hz, 1H), 7.32 - 7.29 (m, 2H), 7.28 - 7.24 (m, 1H), 5.45 (d, *J*=6.8 Hz, 1H), 5.17 - 4.79 (m, 1H), 4.63 (s, 2H), 4.34 (t, *J*=5.1 Hz, 2H), 3.92 (t, *J*=5.3 Hz, 2H), 3.09 - 2.99 (m, 1H), 2.96 - 2.76 (m, 2H), 2.72-2.64 (m, 1H), 2.09 - 1.96 (m, 2H), 1.92 - 1.60 (m, 5H), 1.57 - 1.45 (m, 2H).

Example 84:

N-benzyl-3-cyclopentyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

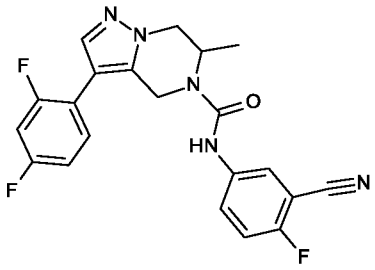


Preparation of Example 84:

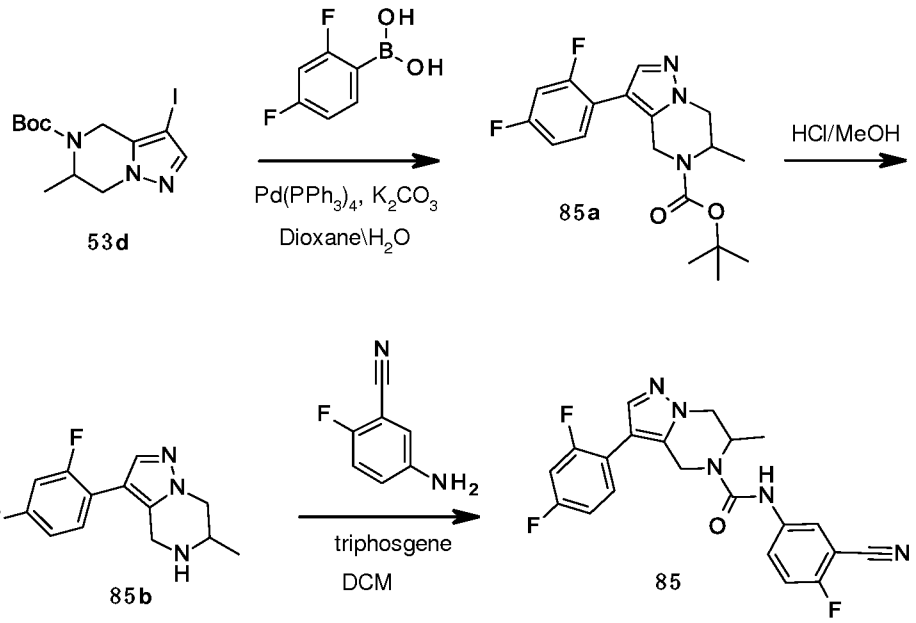
The title compound was prepared in analogy to the preparation of Example **11** by using benzylamine instead of 3-(trifluoromethyl)aniline and 3-cyclopentyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **26c**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **84** was obtained as a white solid. LCMS ($M+H^+$): 325. ^1H NMR (400 MHz, chloroform-d) δ ppm 7.45 (s, 1H), 7.39 - 7.24 (m, 5H), 5.29 (br. s, 1H), 4.66 - 4.56 (m, 2H), 4.50 - 4.37 (m, 2H), 4.27 (t, *J*=5.1 Hz, 2H), 3.88 (t, *J*=5.1 Hz, 2H), 2.86 - 2.72 (m, 1H), 2.07 - 1.97 (m, 2H), 1.84 - 1.62 (m, 4H), 1.56 - 1.42 (m, 2H).

Example 85:

N-(3-cyano-4-fluoro-phenyl)-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of 3-(2,4-difluorophenyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound 85b):

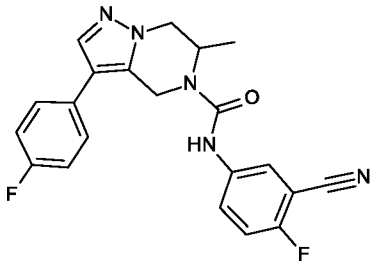
The compound **85b** was prepared in analogy to compound **53f** by using (2,4-difluorophenyl)boronic acid instead of (4-fluorophenyl)boronic acid. Compound **85b** was obtained as a white solid (250 mg). LCMS ($M+H^+$): 250.

Preparation of N-(3-cyano-4-fluoro-phenyl)-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 85):

The title compound was prepared in analogy to the preparation of Example **11** by using 5-amino-2-fluorobenzonitrile instead of 3-(trifluoromethyl)aniline and 3-(2,4-difluorophenyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **85b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **85** was obtained as a white solid (33 mg). LCMS ($M+H^+$): 412. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.09 (s, 1H), 7.94 (dd, *J*=2.7, 5.7 Hz, 1H), 7.82 - 7.75 (m, 1H), 7.73 (d, *J*=1.9 Hz, 1H), 7.56 (dt, *J*=6.7, 8.8 Hz, 1H), 7.45 (t, *J*=9.1 Hz, 1H), 7.40 - 7.36 (m, 1H), 7.19 (dt, *J*=2.3, 8.3 Hz, 1H), 5.08 (d, *J*=16.8 Hz, 1H), 4.99 - 4.89 (m, 1H), 4.53 (d, *J*=16.9 Hz, 1H), 4.32 - 4.14 (m, 2H), 1.20 (d, *J*=6.8 Hz, 3H).

Example 86:

N-(3-cyano-4-fluoro-phenyl)-3-(4-fluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

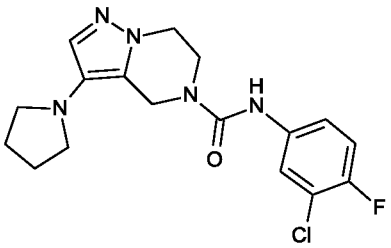


Preparation of Example 86:

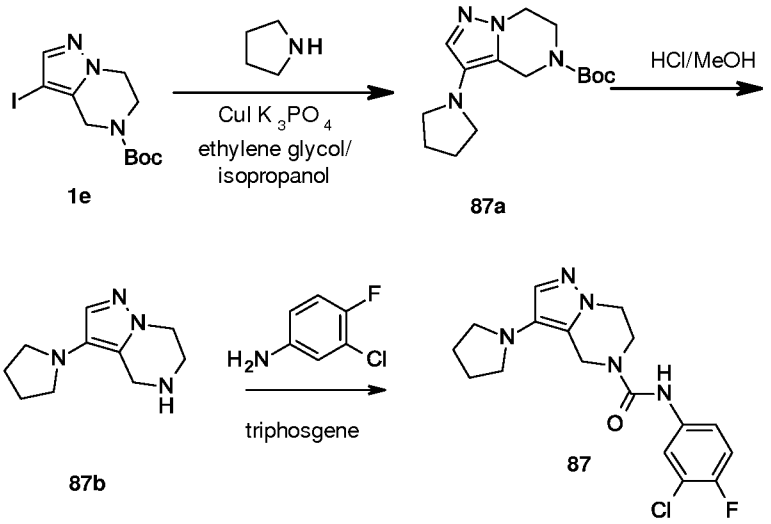
The title compound was prepared in analogy to the preparation of Example **11** by using 5-amino-2-fluoro-benzonitrile instead of 3-trifluoromethylaniline and 3-(4-fluorophenyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **53f**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **86** was obtained as a white solid (12 mg). LCMS ($M+H^+$): 394. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.16 (s, 1H), 7.96 (dd, *J*=2.7, 5.7 Hz, 1H), 7.87 (s, 1H), 7.84 - 7.76 (m, 1H), 7.56 (dd, *J*=5.4, 8.8 Hz, 2H), 7.50 - 7.41 (m, 1H), 7.27 (t, *J*=8.8 Hz, 2H), 5.22 (d, *J*=16.7 Hz, 1H), 5.03 - 4.85 (m, 1H), 4.67 (d, *J*=16.7 Hz, 1H), 4.31 - 4.24 (m, 1H), 4.23 - 4.12 (m, 1H), 1.19 (d, *J*=6.8 Hz, 3H).

Example 87:

N-(3-chloro-4-fluoro-phenyl)-3-pyrrolidin-1-yl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



1e 87a 87b 87

Step 1: **preparation of tert-butyl 3-pyrrolidin-1-yl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 87a)**

To a solution of tert-butyl 3-iodo-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **1e**, 350 mg 1.0 mmol), pyrrolidine (140 mg, 2.0 mmol) and K_3PO_4 (636 mg, 3.0 mmol) in ethane-1,2-diol/propan-2-ol (10 mL, 2:1, v/v) were added CuI (40 mg 0.2 mmol) under N_2. The reaction mixture was stirred at microwave for 2 hours at 120 °C, and then filtered. The filtrate was concentrated, and the residue was purified by column chromatography to afford compound **87a** (100 mg) as a slight yellow oil. LCMS ($M+H^+$): 293.

Step 2: preparation of 3-pyrrolidin-1-yl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound 87b):

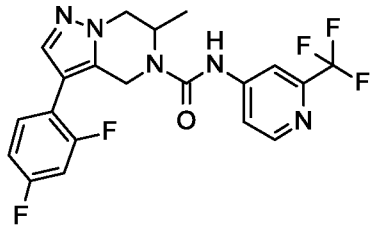
A solution of tert-butyl 3-pyrrolidin-1-yl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **87a**, 88 mg, 0.3 mmol) in HCl/MeOH (20 mL) was stirred at room temperature for 2 hours. Then the reaction mixture was concentrated in *vacuo* to afford compound **87b** (80 mg) as a slight yellow solid. LCMS ($M+H^+$): 293.

Step 3: preparation of N-(3-chloro-4-fluoro-phenyl)-3-pyrrolidin-1-yl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 87):

The title compound was prepared in analogy to the preparation of Example **11** by using 3-chloro-4-fluoroaniline instead of 3-(trifluoromethyl)aniline and 3-pyrrolidin-1-yl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **87b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **87** was obtained as a white solid. LCMS ($M+H^+$): 364. ^1H NMR (400MHz, chloroform-d) δ ppm 7.58 (dd, *J*=2.5, 6.5 Hz, 1H), 7.28 - 7.21 (m, 2H), 7.13 - 7.07 (m, 1H), 6.68 (br. s, 1H), 4.82 (s, 2H), 4.25 (t, *J*=5.4 Hz, 2H), 4.00 (*t*, J=5.5 Hz, 2H), 3.15 (m, 4H), 2.00(m, 4H).

Example 88:

3-(2,4-difluorophenyl)-6-methyl-N-[2-(trifluoromethyl)-4-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

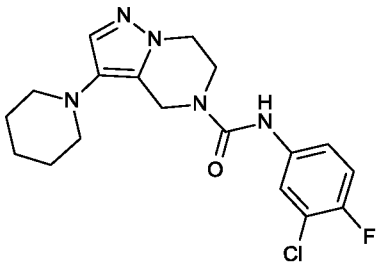


Preparation of Example 88:

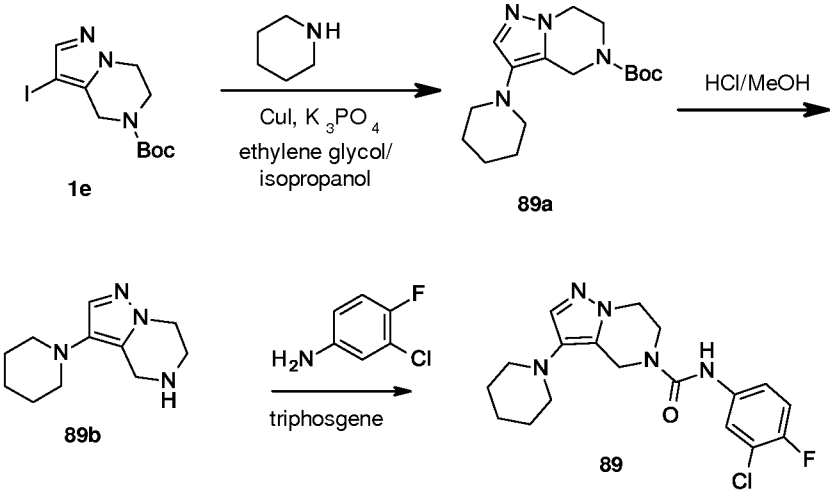
The title compound was prepared in analogy to the preparation of Example **11** by using 2-(trifluoromethyl)pyridin-4-amine instead of 3-(trifluoromethyl)aniline and 3-(2,4-difluorophenyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **85b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **88** was obtained as a white solid (28 mg). LCMS ($M+H^+$): 438. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.55 (s, 1H), 8.52 (d, *J*=5.8 Hz, 1H), 8.02 (d, *J*=1.5 Hz, 1H), 7.78 - 7.70 (m, 2H), 7.62 - 7.52 (m, 1H), 7.43 - 7.33 (m, 1H), 7.20 (dt, *J*=2.3, 8.4 Hz, 1H), 5.12 (d, *J*=16.8 Hz, 1H), 5.01 - 4.89 (m, 1H), 4.57 (d, *J*=17.1 Hz, 1H), 4.35 - 4.28 (m, 1H), 4.27 - 4.19 (m, 1H), 1.22 (d, *J*=6.8 Hz, 3H).

Example 89:

N-(3-chloro-4-fluoro-phenyl)-3-(1-piperidyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of 3-(1-piperidyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound 89b):

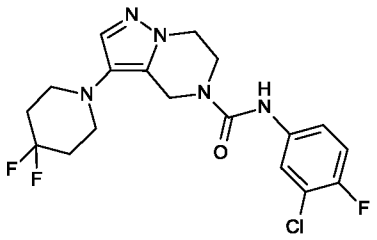
The compound **89b** was prepared in analogy to compound **87b** by using piperidine instead of pyrrolidine. Compound **89b** was obtained as a slight yellow solid (90 mg). LCMS ($M+H^+$): 207.

Preparation of N-(3-chloro-4-fluoro-phenyl)-3-(1-piperidyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 89):

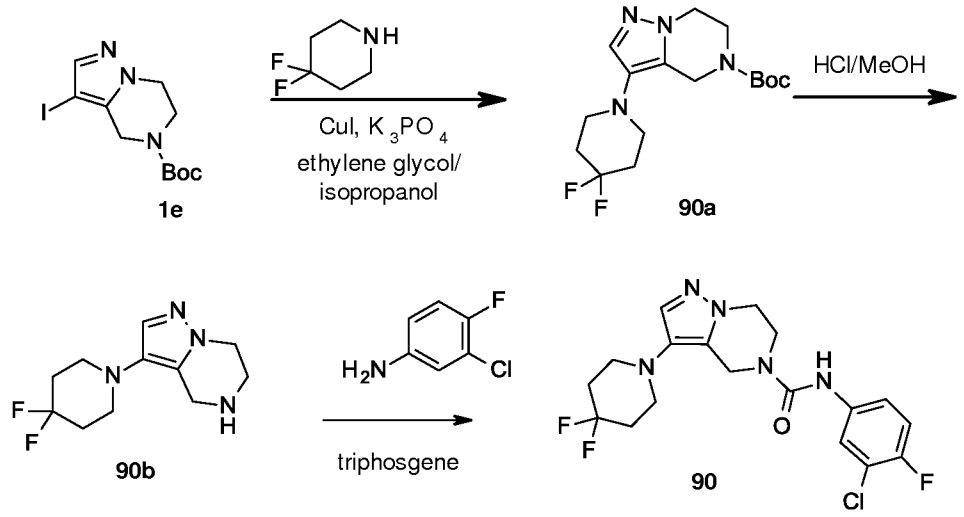
The title compound was prepared in analogy to the preparation of Example **11** by using 3-chloro-4-fluoroaniline instead of 3-(trifluoromethyl)aniline and 3-(1-piperidyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **89b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **89** was obtained as a white solid. LCMS ($M+H^+$): 378. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.03 (br. s, 1H), 7.75 (dd, *J*=2.5, 6.8 Hz, 1H), 7.47 - 7.40 (m, 1H), 7.36 - 7.29 (m, 1H), 7.25 (s, 1H), 4.64 (s, 2H), 4.09 (t, *J*=5.4 Hz, 2H), 3.91 (t, *J*=5.3 Hz, 2H), 2.85 - 2.72 (m, 4H), 1.61 (d, J=5.0 Hz, 4H), 1.48 (d, *J*=5.3 Hz, 2H).

Example 90:

N-(3-chloro-4-fluoro-phenyl)-3-(4,4-difluoro-1-piperidyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of 3-(4,4-difluoro-1-piperidyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound 90b):

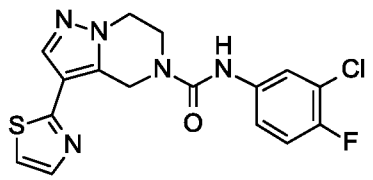
The compound **90b** was prepared in analogy to compound **87b** by using 4,4-difluoropiperidine instead of pyrrolidine. Compound **90b** was obtained as a slight yellow solid (90 mg). LCMS ($M+H^+$): 243.

Preparation of N-(3-chloro-4-fluoro-phenyl)-3-(4,4-difluoro-1-piperidyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 90):

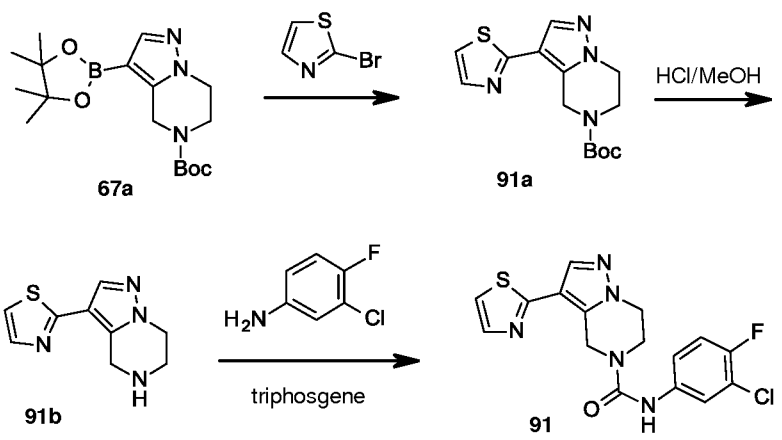
The title compound was prepared in analogy to the preparation of Example **11** by using 3-chloro-4-fluoroaniline instead of 3-(trifluoromethyl)aniline and 3-(4,4-difluoro-1-piperidyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **90b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **90** was obtained as a white solid. LCMS ($M+H^+$): 414. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.03 (s, 1H), 7.75 (dd, *J*=2.5, 6.8 Hz, 1H), 7.50 - 7.39 (m, 1H), 7.37 - 7.23 (m, 2H), 4.66 (s, 2H), 4.15 - 4.04 (m, 2H), 3.92 (t, *J*=5.3 Hz, 2H), 2.96 (t, *J*=5.4 Hz, 4H), 2.16 - 1.96 (m, 4H).

Example 91:

N-(3-chloro-4-fluoro-phenyl)-3-thiazol-2-yl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



67a 91a 91b 91

Preparation of 2-(4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)thiazole (compound 91b):

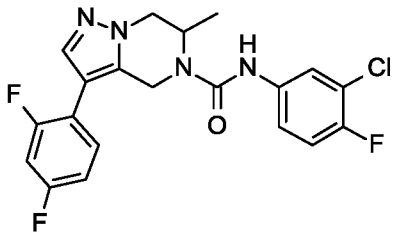
The compound **91b** was prepared in analogy to compound **67c** by using 2-bromothiazole instead of 2-chloro-4-(trifluoromethyl)pyridine. Compound **91b** was obtained as a white solid (250 mg). LCMS ($M+H^+$): 207.

Preparation of N-(3-chloro-4-fluoro-phenyl)-3-thiazol-2-yl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 91):

The title compound was prepared in analogy to the preparation of Example **11** by using 3-chloro-4-fluoroaniline instead of 3-(trifluoromethyl)aniline and 2-(4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)thiazole (compound **91b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **91** was obtained as a white solid (12 mg). LCMS ($M+H^+$): 378. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.20 (s, 1H), 8.00 (s, 1H), 7.85 (d, *J*=3.3 Hz, 1H), 7.74 (dd, *J*=2.6, 6.9 Hz, 1H), 7.64 (d, *J*=3.3 Hz, 1H), 7.43 (dt, *J*=2.6, 4.5 Hz, 1H), 7.36 - 7.28 (m, 1H), 5.00 (s, 2H), 4.26 (t, *J*=5.3 Hz, 2H), 4.02 (t, *J*=5.3 Hz, 2H).

Example 92:

N-(3-chloro-4-fluoro-phenyl)-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

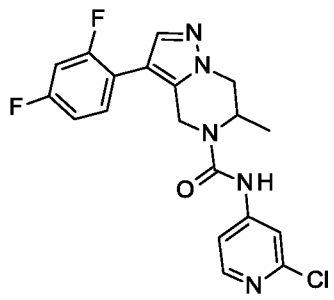


Preparation of Example 92:

The title compound was prepared in analogy to the preparation of Example **11** by using 3-chloro-4-fluoroaniline instead of 3-(trifluoromethyl)aniline and 3-(2,4-difluorophenyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **85b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **92** was obtained as a white solid (24 mg). LCMS ($M+H^+$): 421. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 8.97 (s, 1H), 7.77 - 7.68 (m, 2H), 7.65 - 7.51 (m, 1H), 7.45 - 7.25 (m, 3H), 7.24 - 7.12 (m, 1H), 5.08 (d, *J*=16.8 Hz, 1H), 4.99 - 4.87 (m, 1H), 4.51 (d, *J*=16.8 Hz, 1H), 4.32 - 4.24 (m, 1H), 4.24 - 4.16 (m, 1H), 1.19 (d, *J*=6.8 Hz, 3H).

Example 93:

N-(2-chloro-4-pyridyl)-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

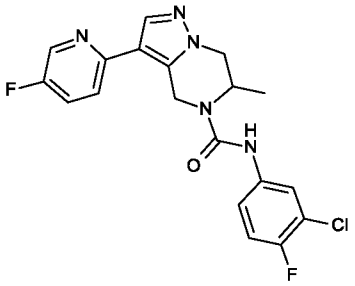


Preparation of Example 93:

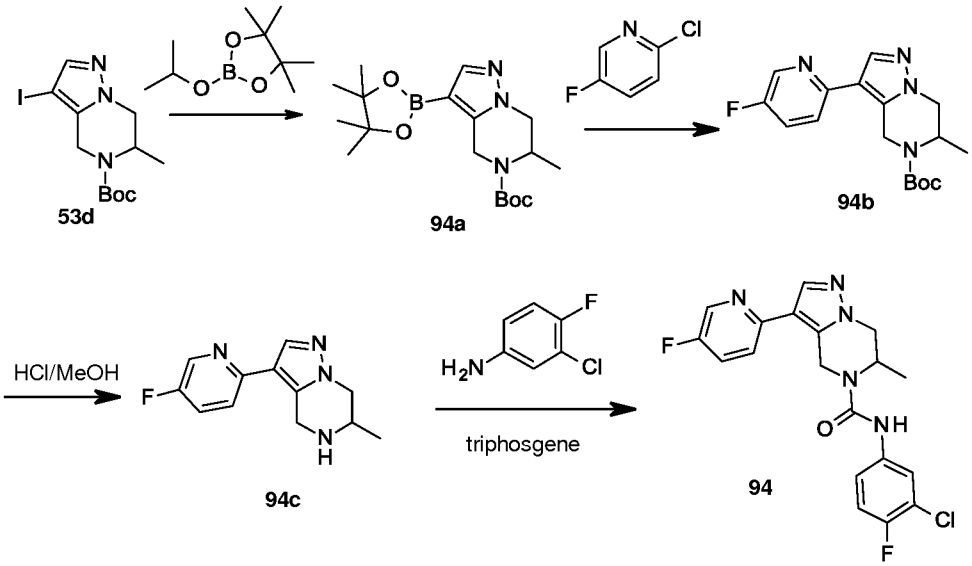
The title compound was prepared in analogy to the preparation of Example **11** by using 2-chloro-pyridin-4-amine instead of 3-(trifluoromethyl)aniline and 3-(2,4-difluorophenyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **85b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **93** was obtained as a white solid (10 mg). LCMS ($M+H^+$): 404. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.51 (s, 1H), 8.17 (d, *J*=5.5 Hz, 1H), 7.73 (s, 1H), 7.64 (s, 1H), 7.57 (d, *J*=7.8 Hz, 1H), 7.47 (s, 1H), 7.42 - 7.32 (m, 1H), 7.19 (s, 1H), 5.10 (d, *J*=17.3 Hz, 1H), 4.94 (m, 1H), 4.55 (d, *J*=16.6 Hz, 1H), 4.35 - 4.17 (m, 2H), 1.26 - 1.16 (m, 3H).

Example 94:

N-(3-chloro-4-fluoro-phenyl)-3-(5-fluoro-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme



Preparation of 3-(5-fluoro-2-pyridyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound 94c):

The compound **94c** was prepared in analogy to compound **67c** by using 2-chloro-5-fluoro-pyridine instead of 2-chloro-4-(trifluoromethyl)pyridine and tert-butyl 3-iodo-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **53d**) instead of tert-butyl 3-iodo-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **1e**). Compound **94c** was obtained as a white solid (250 mg). LCMS ($M+H^+$): 233.

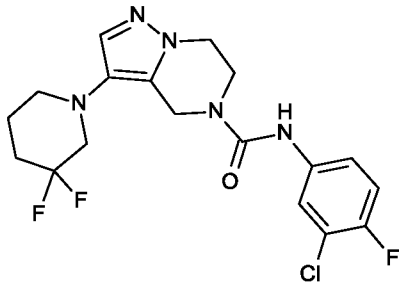
Preparation of N-(3-chloro-4-fluoro-phenyl)-3-(5-fluoro-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 94):

The title compound was prepared in analogy to the preparation of Example **11** by using 3-chloro-4-fluoroaniline instead of 3-(trifluoromethyl)aniline and 3-(5-fluoro-2-pyridyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **94b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **94** was obtained as a white solid (48 mg). LCMS ($M+H^+$): 404. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.03 (s, 1H), 8.58 (d, *J*=2.9 Hz, 1H), 8.14 (s, 1H), 7.84 - 7.72 (m, 3H), 7.47 - 7.40 (m, 1H), 7.37 - 7.30 (m, 1H), 5.44

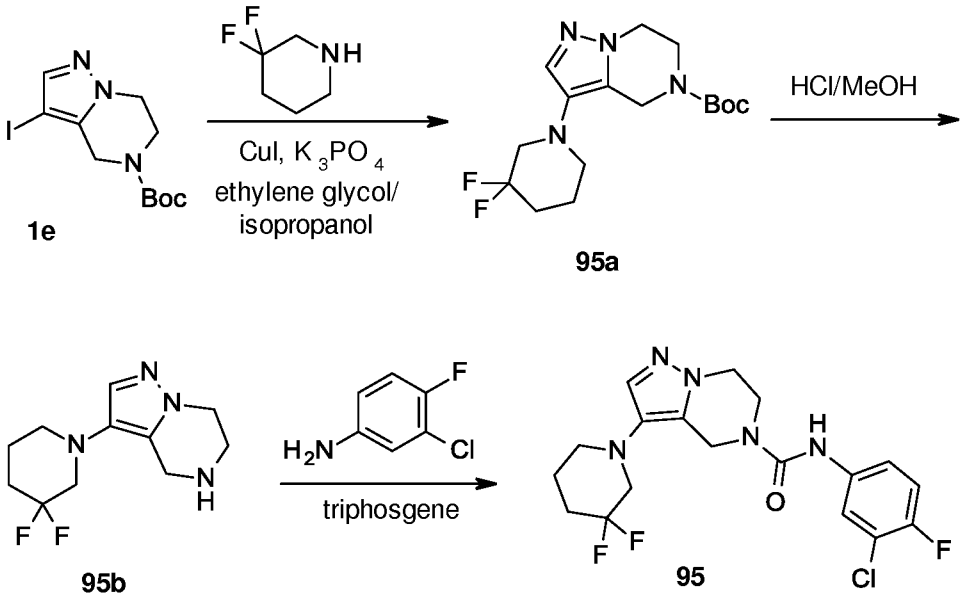
(d, *J*=18.1 Hz, 1H), 4.93 - 4.84 (m, 1H), 4.62 (d, *J*=18.2 Hz, 1H), 4.28 (d, *J*=4.4 Hz, 1H), 4.23 - 4.17 (m, 1H), 1.18 (d, *J*=6.8 Hz, 3H).

Example 95:

N-(3-chloro-4-fluoro-phenyl)-3-(3,3-difluoro-1-piperidyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of 3-(3,3-difluoro-1-piperidyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound 95b):

The compound **95b** was prepared in analogy to compound **87b** by using 4,4-difluoropiperidine instead of pyrrolidine. Compound **95b** was afforded as a slight yellow solid (90 mg). LCMS ($M+H^+$): 243.

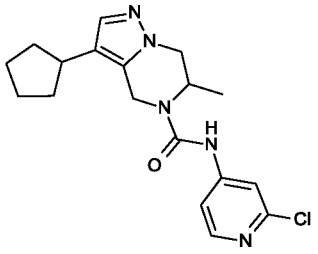
Preparation of N-(3-chloro-4-fluoro-phenyl)-3-(3,3-difluoro-1-piperidyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 95):

The title compound was prepared in analogy to the preparation of Example **11** by using 3-chloro-4-fluoroaniline instead of 3-(trifluoromethyl)aniline and 3-(3,3-difluoro-1-piperidyl)-

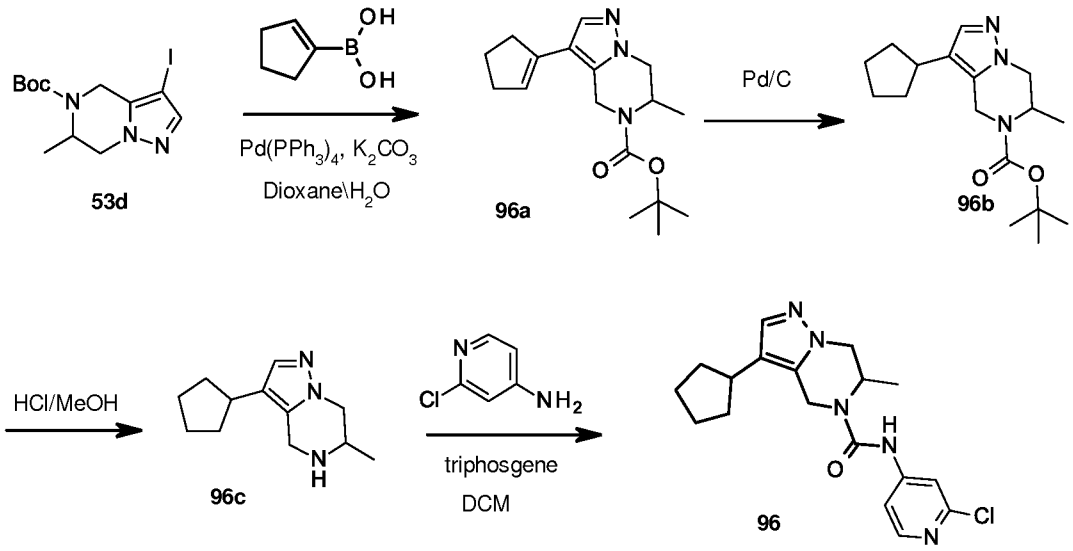
4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **95b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **95** was obtained as a white solid (10 mg). LCMS ($M+H^+$): 414. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.09 (s, 1H), 7.75 (dd, *J*=2.5, 7.0 Hz, 1H), 7.44 (d, *J*=7.5 Hz, 1H), 7.35 - 7.28 (m, 2H), 4.65 (s, 2H), 4.10 (d, *J*=5.0 Hz, 2H), 3.93 (d, *J*=5.3 Hz, 2H), 3.09 (t, *J*=11.5 Hz, 2H), 2.84 (m, 2H), 1.97 (dd, *J*=6.5, 13.6 Hz, 2H), 1.78 (m, 2H).

Example 96:

N-(2-chloro-4-pyridyl)-3-cyclopentyl-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of 3-cyclopentyl-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound 96c)

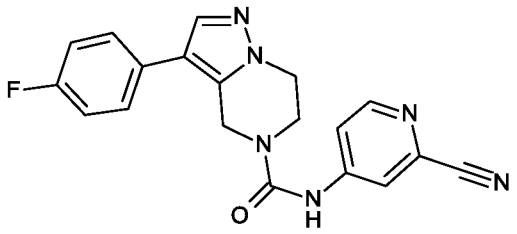
The compound **96c** was prepared in analogy to compound **26c** by using tert-butyl 3-iodo-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **53d**) instead of tert-butyl 3-iodo-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **1e**). Compound **96c** was obtained as a slight yellow solid (90 mg). LCMS ($M+H^+$): 257.

Preparation of N-(2-chloro-4-pyridyl)-3-cyclopentyl-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 96)

The title compound was prepared in analogy to the preparation of Example **11** by using 2-chloro-pyridin-4-amine instead of 3-(trifluoromethyl)aniline and 3-cyclopentyl-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **96c**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **96** was obtained as a white solid (8 mg). LCMS ($M+H^+$): 360. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.33 (s, 1H), 8.19 (d, *J*=5.8 Hz, 1H), 7.68 (d, *J*=1.8 Hz, 1H), 7.50 (dd, *J*=1.8, 5.7 Hz, 1H), 7.34 (s, 1H), 5.00 (d, *J*=16.3 Hz, 1H), 4.94 - 4.82 (m, 1H), 4.40 (d, *J*=16.2 Hz, 1H), 4.22 - 4.13 (m, 1H), 4.12 - 4.05 (m, 1H), 2.92 - 2.78 (m, 1H), 1.99 (m, 2H), 1.79 - 1.69 (m, 2H), 1.67 - 1.55 (m, 2H), 1.47 (m, 2H), 1.11 (d, J=6.8 Hz, 3H).

Example 97:

N-(2-cyano-4-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

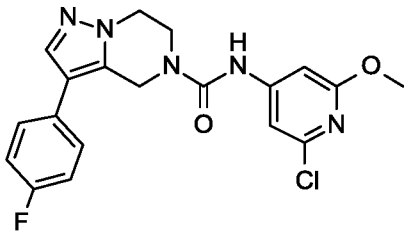


Preparation of Example 97:

The title compound was prepared in analogy to the preparation of Example **11** by using 4-aminopyridine-2-carbonitrile instead of 3-(trifluoromethyl)aniline. Example **97** was obtained as a white solid (24 mg). LCMS ($M+H^+$): 363. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.75 (br.s, 1 H), 8.50 (d, *J*=5.6 Hz, 1H), 8.05 (s, 1H), 7.84 (s, 1H), 7.79 - 7.70 (m, 1H), 7.50 (dd, *J*=5.5, 8.6 Hz, 2H), 7.28 (t, *J*=8.8 Hz, 2H), 4.98 (s, 2H), 4.25 (t, *J*=5.1 Hz, 2H), 4.04 (t, *J*=5.1 Hz, 2H).

Example 98:

N-(2-chloro-6-methoxy-4-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

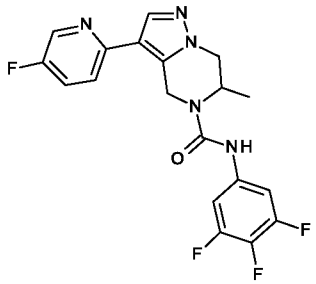


Preparation of Example 98:

The title compound was prepared in analogy to the preparation of Example **11** by using 2-chloro-6-methoxy-pyridin-4-amine instead of 3-(trifluoromethyl)aniline. Example **98** was obtained as a white solid. LCMS ($M+H^+$): 402. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.45 (br. s, 1H), 7.83 (s, 1H), 7.49 (dd, *J*=5.5, 8.7 Hz, 2H), 7.34 - 7.20 (m, 3H), 6.96 (s, 1H), 4.94 (s, 2H), 4.23 (t, *J*=5.1 Hz, 2H), 4.01 (t, *J*=5.3 Hz, 2H), 3.80 (s, 3H).

Example 99:

3-(5-fluoro-2-pyridyl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

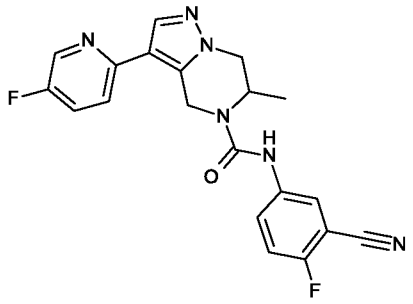


Preparation of Example 99:

The title compound was prepared in analogy to the preparation of Example **11** by using 3,4,5-trifluoroaniline instead of 3-(trifluoromethyl)aniline and 3-(5-fluoro-2-pyridyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **94b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **99** was obtained as a white solid (17 mg). LCMS ($M+H^+$): 406. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.18 (s, 1H), 8.59 (d, *J*=2.8 Hz, 1H), 8.14 (s, 1H), 7.85 - 7.73 (m, 2H), 7.43 (dd, *J*=6.6, 10.7 Hz, 2H), 5.47 - 5.38 (m, 1H), 4.92 - 4.85 (m, 1H), 4.69 - 4.59 (m, 1H), 4.36 - 4.27 (m, 1H), 4.23 - 4.17 (m, 1H), 1.18 (d, J=6.8 Hz, 3H).

Example 100:

N-(3-cyano-4-fluoro-phenyl)-3-(5-fluoro-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

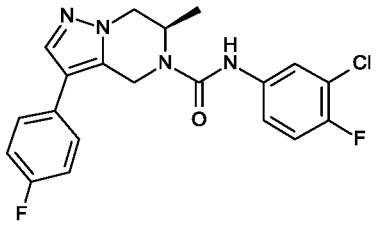


Preparation of Example 100:

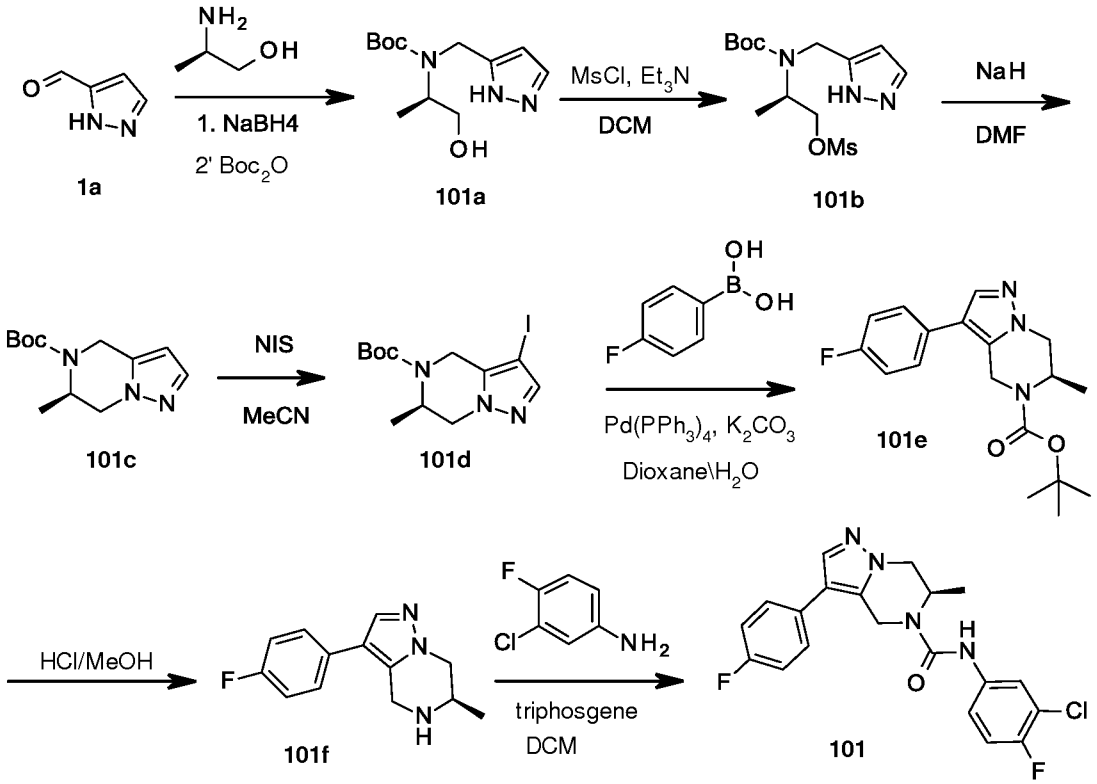
The title compound was prepared in analogy to the preparation of Example **11** by using 5-amino-2-fluoro-benzonitrile instead of 3-(trifluoromethyl)aniline and 3-(5-fluoro-2-pyridyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **94b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **100** was obtained as a white solid. LCMS ($M+H^+$): 395. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.22 (s, 1H), 8.58 (d, *J*=2.8 Hz, 1H), 8.14 (s, 1H), 7.98 - 7.94 (m, 1H), 7.84 - 7.74 (m, 3H), 7.46 (s, 1H), 5.45 (d, *J*=18.1 Hz, 1H), 4.95 - 4.87 (m, 1H), 4.69 - 4.605 (m, 1H), 4.34 - 4.28 (m, 1H), 4.23 - 4.18 (m, 1H), 1.19 (d, *J*=6.8 Hz, 3H).

Example 101:

(6R)-N-(3-chloro-4-fluoro-phenyl)-3-(4-fluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of (6R)-3-(4-fluorophenyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound 101f):

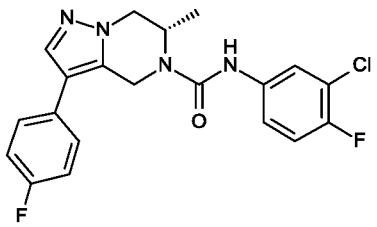
The compound **101f** was prepared in analogy to compound **53f** by using (2R)-2-aminopropan-1-ol instead of 2-aminopropan-1-ol. Compound **101f** was obtained as a white solid. LCMS ($M+H^+$): 232.

Preparation of (6R)-N-(3-chloro-4-fluoro-phenyl)-3-(4-fluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 101):

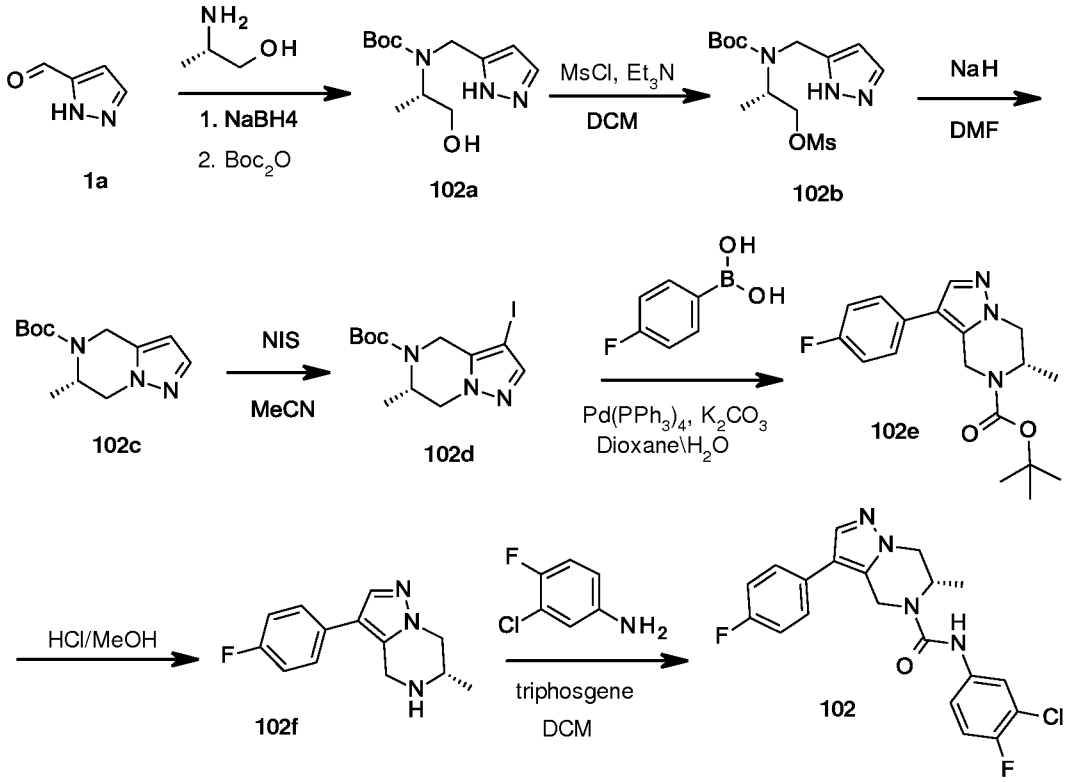
The title compound was prepared in analogy to the preparation of Example **11** by using 3-chloro-4-fluoroaniline instead of 3-trifluoromethylaniline and (6R)-3-(4-fluorophenyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **101f**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **101** was obtained as a white solid (8 mg). LCMS ($M+H^+$): 403. ^1H NMR (400MHz, CD_3OD) δ ppm 7.81 (s, 1H), 7.63 (dd, *J*=2.6, 6.7 Hz, 1H), 7.54 (dd, *J*=5.3, 8.8 Hz, 2H), 7.37 - 7.33 (m, 1H), 7.18 (dt, *J*=1.9, 8.8 Hz, 3H), 5.23 (d, *J*=16.6 Hz, 1H), 5.07 - 4.97 (m, 1H), 4.72 (d, *J*=16.3 Hz, 1H), 4.37 (dd, *J*=4.3, 12.5 Hz, 1H), 4.23 (d, *J*=13.8 Hz, 1H), 1.29 (d, *J*=6.8 Hz, 3H).

Example 102:

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-fluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of (6S)-3-(4-fluorophenyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound 102f):

The compound **102f** was prepared in analogy to compound **53f** by using (2S)-2-aminopropan-1-ol instead of 2-aminopropan-1-ol. Compound **102f** was obtained as a white solid (2 g). LCMS ($M+H^+$): 232.

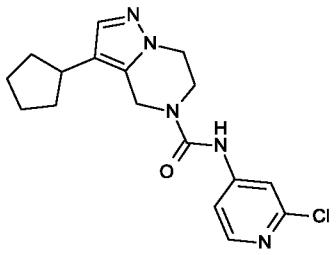
Preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-fluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 102):

The title compound was prepared in analogy to the preparation of Example **11** by using 3-chloro-4-fluoroaniline instead of 3-trifluoromethylaniline and (6S)-3-(4-fluorophenyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **102f**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **102** was obtained as a white solid (8 mg). LCMS ($M+H^+$): 403. ^1H NMR (400MHz, CD_3OD) δ ppm 7.81 (s, 1H), 7.63 (dd, *J*=2.6, 6.7 Hz, 1H), 7.54 (dd, *J*=5.3, 8.8 Hz, 2H), 7.37 - 7.33 (m, 1H), 7.18 (dt, *J*=1.9, 8.8 Hz,

3H), 5.23 (d, *J*=16.6 Hz, 1H), 5.07 - 4.97 (m, 1H), 4.72 (d, *J*=16.3 Hz, 1H), 4.37 (dd, *J*=4.3, 12.5 Hz, 1H), 4.23 (d, *J*=13.8 Hz, 1H), 1.29 (d, *J*=6.8 Hz, 3H).

Example 103:

N-(2-chloro-4-pyridyl)-3-cyclopentyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

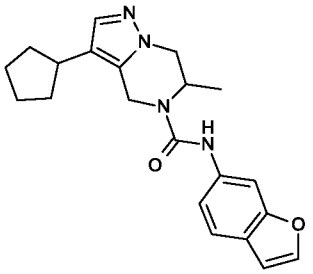


Preparation of Example 103:

The title compound was prepared in analogy to the preparation of Example **11** by using 2-chloro-pyridin-4-amine instead of 3-(trifluoromethyl)aniline and 3-cyclopentyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **26c**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **103** was obtained as a white solid (15 mg). LCMS ($M+H^+$): 346. ^1H NMR (400 MHz, DMSO-d_6) δ ppm 9.44 (s, 1H), 8.18 (d, *J*=5.6 Hz, 1H), 7.66 (d, *J*=1.5 Hz, 1H), 7.48 (dd, *J*=1.6, 5.6 Hz, 1H), 7.32 (s, 1H), 4.71 (s, 2H), 4.13 (t, *J*=5.2 Hz, 2H), 3.95 (t, *J*=5.1 Hz, 2H), 2.89 - 2.76 (m, 1H), 1.96 (d, *J*=6.8 Hz, 2H), 1.78 - 1.55 (m, 4H), 1.52 - 1.40 (m, 2H).

Example 104:

N-(benzofuran-6-yl)-3-cyclopentyl-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



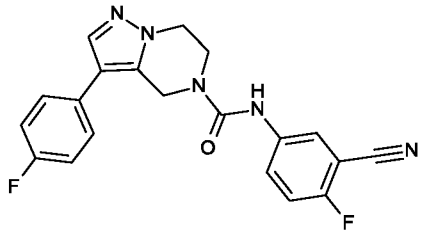
Preparation of Example 104:

The title compound was prepared in analogy to the preparation of Example **11** by using benzofuran-6-amine instead of 3-(trifluoromethyl)aniline and 3-cyclopentyl-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **96c**) instead of 3-(4-fluorophenyl)-4,5,6,7-

tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **104** was obtained as a white solid. LCMS ($M+H^+$): 365. ^1H NMR (400 MHz, chloroform-d) δ ppm 7.80 (s, 1H), 7.61 (d, *J*=2.3 Hz, 1H), 7.52 (d, *J*=8.3 Hz, 1H), 7.41 (s, 1H), 7.14 (dd, *J*=1.9, 8.4 Hz, 1H), 6.74 (d, *J*=1.3 Hz, 1H), 6.61 (s, 1H), 4.99 - 4.83 (m, 2H), 4.52 (d, *J*=15.3 Hz, 1H), 4.31 (dd, *J*=4.1, 12.7 Hz, 1H), 4.16 (d, *J*=12.5 Hz, 1H), 2.90 - 2.81 (m, 1H), 2.10 - 1.99 (m, 2H), 1.83 - 1.55 (m, 6H), 1.25 (d, *J*=6.8 Hz, 3H).

Example 105:

N-(3-cyano-4-fluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

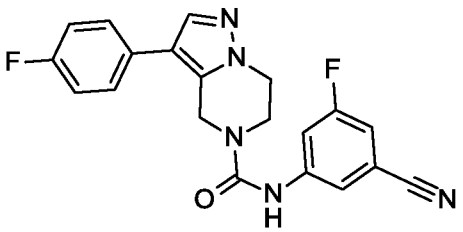


Preparation of Example 105:

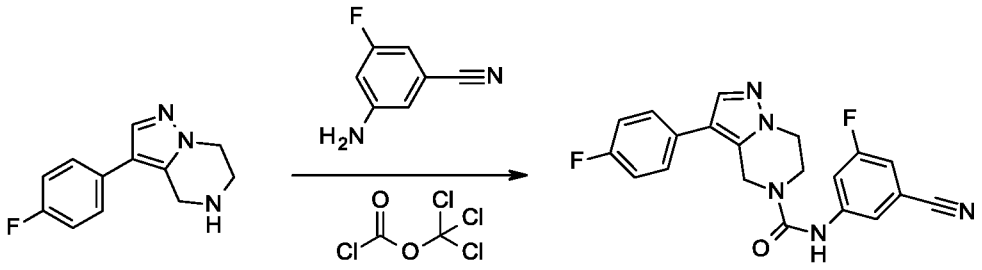
The title compound was prepared in analogy to the preparation of Example **11** by using 5-amino-2-fluoro-benzonitrile instead of 3-(trifluoromethyl)aniline. Example **105** was obtained as a white solid (22 mg). LCMS ($M+H^+$): 380. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.28 (s, 1H), 7.95 (dd, *J*=2.6, 5.6 Hz, 1H), 7.86 - 7.76 (m, 2H), 7.54 - 7.40 (m, 3H), 7.27 (t, *J*=8.8 Hz, 2H), 4.95 (s, 2H), 4.23 (t, *J*=5.1 Hz, 2H), 4.02 (t, *J*=5.3 Hz, 2H).

Example 106:

N-(3-cyano-5-fluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



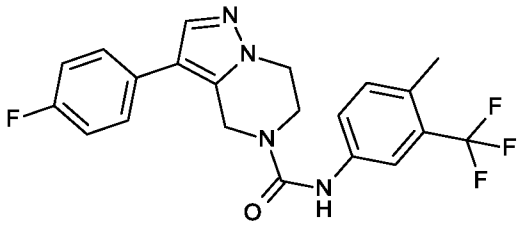
11b 106

Preparation of Example 106:

To a solution of 3-amino-5-fluoro-benzonitrile (30 mg, 0.2 mmol) in DCM (1 mL), was added trichloromethyl carbonochloridate (19 mg, 0.1 mmol). Then the reaction mixture was stirred at room temperature for 10 mins, to previous reaction mixture was added another mixture of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**, 22 mg, 0.1 mmol) and DIPEA (65 mg, 0.5 mmol) in DCM (1 mL) slowly. The resulting mixture was stirred at room temperature for 5 min and then diluted with EtOAc (10 mL), washed with water (5 mL), brine (5 mL). The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by prep-HPLC to afford Example **106** (4 mg) as a white solid. LCMS ($M+H^+$): 380. ^1H NMR (400MHz, CD_3OD) δ ppm 7.77 (s, 1H), 7.71 - 7.60 (m, 2H), 7.49 (dd, *J*=5.3, 8.8 Hz, 2H), 7.25 - 7.12 (m, 3H), 5.00 (s, 2H), 4.32 (t, *J*=5.5 Hz, 2H), 4.11 (t, *J*=5.5 Hz, 2H).

Example 107:

3-(4-fluorophenyl)-N-[4-methyl-3-(trifluoromethyl)phenyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



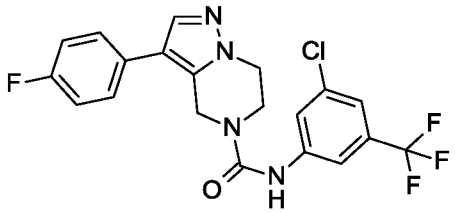
Preparation of Example 107:

The title compound was prepared in analogy to the preparation of Example **106** by using 4-methyl-3-trifluoromethyl-aniline instead of 3-amino-5-fluoro-benzonitrile. Example **107** was obtained as a white solid (30 mg). LCMS ($M+H^+$): 419. ^1H NMR (400MHz, CD_3OD) δ ppm 7.79 - 7.71 (m, 2H), 7.54 (dd, *J*=2.1, 8.4 Hz, 1H), 7.49 (dd, *J*=5.3, 8.8 Hz, 2H), 7.28 (d, *J*=8.3 Hz,

1H), 7.22 - 7.11 (m, 2H), 4.98 (s, 2H), 4.31 (t, *J*=5.4 Hz, 2H), 4.09 (t, *J*=5.4 Hz, 2H), 2.42 (d, *J*=1.5 Hz, 3H).

Example 108:

N-[3-chloro-5-(trifluoromethyl)phenyl]-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

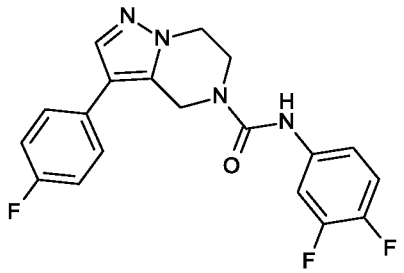


Preparation of Example 108:

The title compound was prepared in analogy to the preparation of Example **106** by using 3-chloro-5-(trifluoromethyl)aniline instead of 3-amino-5-fluoro-benzonitrile. Example **108** was obtained as a white solid (10 mg). LCMS ($M+H^+$): 439. ^1H NMR (400MHz, CD_3OD) δ ppm 7.87 - 7.81 (m, 1H), 7.80 - 7.72 (m, 2H), 7.49 (dd, *J*=5.3, 8.8 Hz, 2H), 7.33 (s, 1H), 7.18 (t, *J*=8.9 Hz, 2H), 5.00 (s, 2H), 4.32 (t, *J*=5.4 Hz, 2H), 4.11 (t, *J*=5.4 Hz, 2H).

Example 109:

N-(3,4-difluorophenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

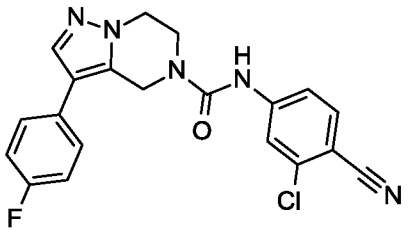


Preparation of Example 109:

The title compound was prepared in analogy to the preparation of Example **106** by using 3,4-difluoroaniline instead of 3-amino-5-fluoro-benzonitrile. Example **109** was obtained as a white solid (9 mg). LCMS ($M+H^+$): 373. ^1H NMR (400MHz, CD_3OD) δ ppm 7.77 (s, 1H), 7.53 - 7.41 (m, 3H), 7.23 - 7.10 (m, 4H), 4.97 (s, 2H), 4.30 (t, *J*=5.4 Hz, 2H), 4.10 (t, *J*=5.4 Hz, 2H).

Example 110:

N-(3-chloro-4-cyano-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

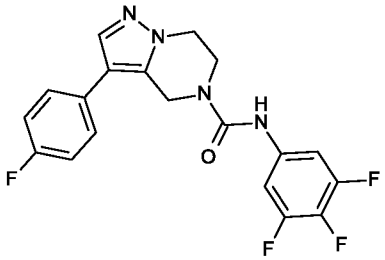


Preparation of Example 110:

The title compound was prepared in analogy to the preparation of Example **106** by using 4-amino-2-chloro-benzonitrile instead of 3-amino-5-fluoro-benzonitrile. Example **110** was obtained as a white solid (5 mg). LCMS ($M+H^+$): 396. ^1H NMR (400MHz, CD_3OD) δ ppm 7.89 - 7.84 (m, 1H), 7.77 (s, 1H), 7.68 (d, *J*=8.5 Hz, 1H), 7.58 - 7.44 (m, 3H), 7.18 (t, *J*=8.8 Hz, 2H), 5.00 (s, 2H), 4.30 (t, *J*=5.4 Hz, 2H), 4.10 (t, *J*=5.4 Hz, 2H).

Example 111:

3-(4-fluorophenyl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

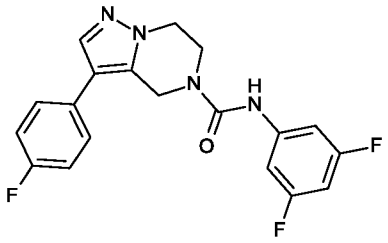


Preparation of Example 111:

The title compound was prepared in analogy to the preparation of Example **106** by using 3,4,5-trifluoroaniline instead of 3-amino-5-fluoro-benzonitrile. Example **111** was obtained as a white solid (5 mg). LCMS ($M+H^+$): 391. ^1H NMR (400MHz, CD_3OD) δ ppm 7.77 (s, 1H), 7.49 (dd, *J*=5.3, 8.8 Hz, 2H), 7.27 (dd, *J*=6.5, 10.3 Hz, 2H), 7.18 (t, *J*=8.9 Hz, 2H), 4.97 (s, 2H), 4.30 (t, *J*=5.4 Hz, 2H), 4.08 (t, *J*=5.4 Hz, 2H).

Example 112:

N-(3,5-difluorophenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

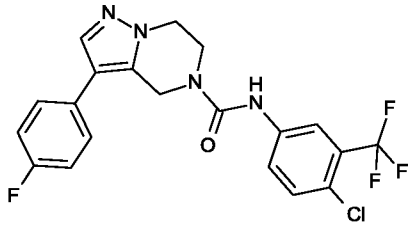


Preparation of Example 112:

The title compound was prepared in analogy to the preparation of Example **106** by using 3,5-difluoroaniline instead of 3-amino-5-fluoro-benzonitrile. Example **112** was obtained as a white solid (10 mg). LCMS ($M+H^+$): 373. ^1H NMR (400MHz, CD_3OD) δ ppm 7.77 (s, 1H), 7.49 (dd, *J*=5.4, 8.9 Hz, 2H), 7.23 - 7.08 (m, 4H), 6.64 - 6.49 (m, 1H), 4.98 (s, 2H), 4.31 (t, *J*=5.4 Hz, 2H), 4.10 (t, *J*=5.4 Hz, 2H).

Example 113:

N-[4-chloro-3-(trifluoromethyl)phenyl]-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

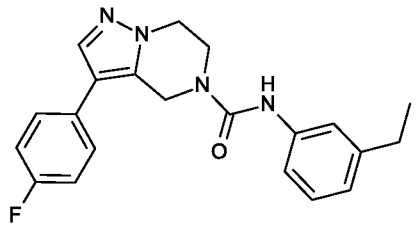


Preparation of Example 113:

The title compound was prepared in analogy to the preparation of Example **106** by using 4-chloro-3-(trifluoromethyl)aniline instead of 3-amino-5-fluoro-benzonitrile. Example **113** was obtained as a white solid (12 mg). LCMS ($M+H^+$): 439. ^1H NMR (400MHz, CD_3OD) δ ppm 7.93 (d, *J*=2.5 Hz, 1H), 7.77 (s, 1H), 7.69 (dd, *J*=2.5, 8.8 Hz, 1H), 7.55 - 7.43 (m, 3H), 7.18 (t, *J*=8.8 Hz, 2H), 5.00 (s, 2H), 4.32 (t, *J*=5.4 Hz, 2H), 4.12 (t, *J*=5.4 Hz, 2H).

Example 114:

N-(3-ethylphenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

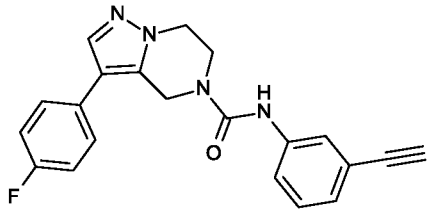


Preparation of Example 114:

The title compound was prepared in analogy to the preparation of Example **106** by using 3-ethylaniline instead of 3-amino-5-fluoro-benzonitrile. Example **114** was obtained as a white solid (11 mg). LCMS ($M+H^+$): 365. ^1H NMR (400MHz, CD_3OD) δ ppm 7.77 (s, 1H), 7.58 - 7.42 (m, 2H), 7.32 - 7.07 (m, 5H), 6.99 - 6.81 (m, 1H), 4.98 (s, 2H), 4.31 (t, *J*=5.4 Hz, 2H), 4.09 (t, *J*=5.4 Hz, 2H), 2.63 (q, *J*=7.5 Hz, 2H), 1.24 (t, *J*=7.7 Hz, 3H).

Example 115:

N-(3-ethynylphenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

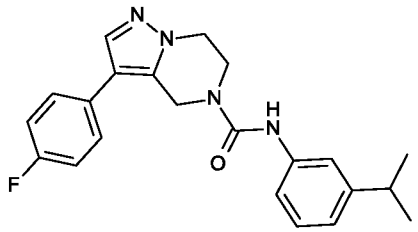


Preparation of Example 115:

The title compound was prepared in analogy to the preparation of Example **106** by using 3-ethynylaniline instead of 3-amino-5-fluoro-benzonitrile. Example **115** was obtained as a white solid (12 mg). LCMS ($M+H^+$): 361. ^1H NMR (400MHz, CD_3OD) δ ppm 7.77 (s, 1H), 7.56 (t, *J*=1.8 Hz, 1H), 7.53 - 7.46 (m, 2H), 7.45 - 7.40 (m, 1H), 7.27 (t, *J*=8.0 Hz, 1H), 7.22 - 7.12 (m, 3H), 4.98 (s, 2H), 4.31 (t, *J*=5.4 Hz, 2H), 4.10 (t, *J*=5.5 Hz, 2H), 3.47 (s, 1H).

Example 116:

3-(4-fluorophenyl)-N-(3-isopropylphenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

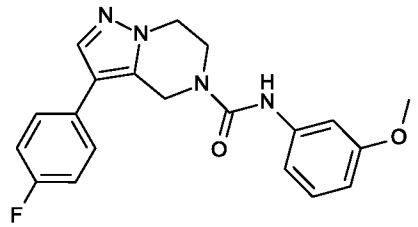


Preparation of Example 116:

The title compound was prepared in analogy to the preparation of Example **106** by using 3-isopropylaniline instead of 3-amino-5-fluoro-benzonitrile. Example **116** was obtained as a white solid (17 mg). LCMS ($M+H^+$): 379. ^1H NMR (400MHz, CD_3OD) δ ppm 7.77 (s, 1H), 7.50 (dd, *J*=5.4, 8.9 Hz, 2H), 7.28 (s, 1H), 7.25 - 7.12 (m, 4H), 7.01 - 6.90 (m, 1H), 4.98 (s, 2H), 4.31 (t, *J*=5.5 Hz, 2H), 4.10 (t, *J*=5.5 Hz, 2H), 2.91 - 2.83 (m, 1H), 1.25 (d, *J*=7.0 Hz, 6H).

Example 117:

3-(4-fluorophenyl)-N-(3-methoxyphenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

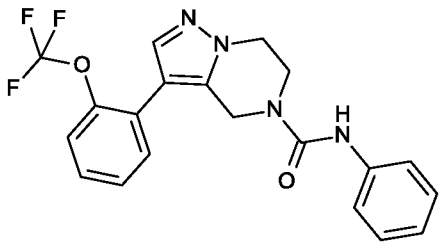


Preparation of Example 117:

The title compound was prepared in analogy to the preparation of Example **106** by using 3-methoxyl aniline instead of 3-amino-5-fluoro-benzonitrile. Example **117** was obtained as a white solid (10 mg). LCMS ($M+H^+$): 367. ^1H NMR (400MHz, CD_3OD) δ ppm 7.77 (s, 1H), 7.49 (dd, *J*=5.3, 8.8 Hz, 2H), 7.18 (dt, *J*=3.6, 8.5 Hz, 3H), 7.07 (t, *J*=2.2 Hz, 1H), 6.96 (dd, *J*=1.2, 8.1 Hz, 1H), 6.63 (dd, *J*=1.8, 8.2 Hz, 1H), 4.97 (s, 2H), 4.31 (t, *J*=5.5 Hz, 2H), 4.09 (t, *J*=5.5 Hz, 2H), 3.78 (s, 3H).

Example 118:

N-phenyl-3-[2-(trifluoromethoxy)phenyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

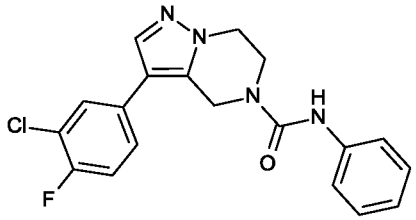


Preparation of Example 118:

The title compound was prepared in analogy to the preparation of Example **1** by using 2-(trifluoromethoxy)phenyl-boronic acid instead of (4-fluorophenyl)boronic acid. Example **118** was obtained as a white solid (21 mg). LCMS ($M+H^+$): 403. ^1H NMR (400MHz, CD_3OD) δ ppm 7.69 (s, 1H), 7.56 - 7.48 (m, 1H), 7.47 - 7.42 (m, 3H), 7.41 - 7.34 (m, 2H), 7.33 - 7.24 (m, 2H), 7.10 - 7.01 (m, 1H), 4.84 (s, 2H), 4.34 (t, *J*=5.5 Hz, 2H), 4.10 (t, *J*=5.5 Hz, 2H).

Example 119:

3-(3-chloro-4-fluoro-phenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

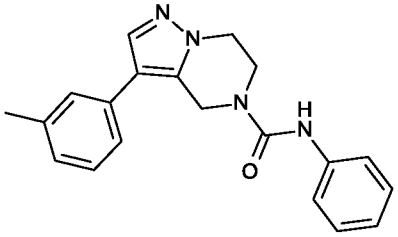


Preparation of Example 119:

The title compound was prepared in analogy to the preparation of Example **1** by using (3-chloro-4-fluorophenyl)boronic acid instead of (4-fluorophenyl)boronic acid. Example **119** was obtained as a white solid (32 mg). LCMS ($M+H^+$): 371. ^1H NMR (400MHz, CD_3OD) δ ppm 7.80 (s, 1H), 7.59 (dd, *J*=1.9, 7.0 Hz, 1H), 7.49 - 7.35 (m, 3H), 7.35 - 7.23 (m, 3H), 7.12 - 7.01 (m, 1H), 4.98 (s, 2H), 4.31 (t, *J*=5.4 Hz, 2H), 4.09 (t, *J*=5.4 Hz, 2H).

Example 120:

3-(m-tolyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

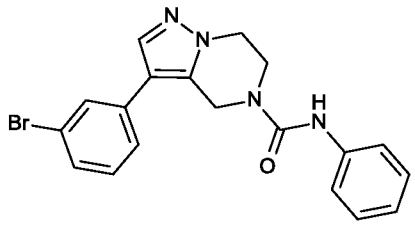


Preparation of Example 120:

The title compound was prepared in analogy to the preparation of Example **1** by using (3-methyl-phenyl)boronic acid instead of (4-fluorophenyl)boronic acid. Example **120** was obtained as a white solid. LCMS ($M+H^+$): 333. ^1H NMR (400MHz, CD_3OD) δ ppm 7.77 (s, 1H), 7.43 - 7.36 (m, 2H), 7.34 - 7.21 (m, 5H), 7.15 - 7.01 (m, 2H), 4.99 (s, 2H), 4.31 (t, *J*=5.5 Hz, 2H), 4.09 (t, *J*=5.5 Hz, 2H), 2.40 (s, 3H).

Example 121:

3-(3-bromophenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

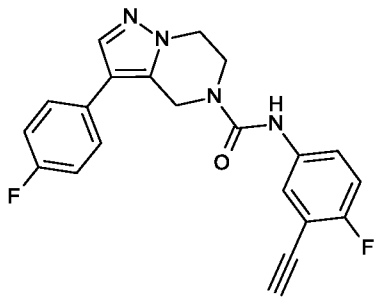


Preparation of Example 121:

The title compound was prepared in analogy to the preparation of Example **1** by using (3-bromophenyl)boronic acid instead of (4-fluorophenyl)boronic acid. Example **121** was obtained as a white solid (14 mg). LCMS ($M+H^+$): 397. ^1H NMR (400MHz, CD_3OD) δ ppm 7.82 (s, 1H), 7.65 (s, 1H), 7.50 - 7.42 (m, 2H), 7.41 - 7.34 (m, 3H), 7.33 - 7.24 (m, 2H), 7.10 - 7.01 (m, 1H), 5.00 (s, 2H), 4.32 (t, *J*=5.5 Hz, 2H), 4.10 (t, *J*=5.4 Hz, 2H).

Example 122:

N-(3-ethynyl-4-fluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



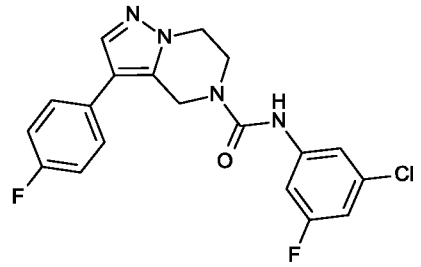
Preparation of Example 122:

The title compound was prepared in analogy to the preparation of Example **106** by using 3-ethynyl-4-fluoro-aniline instead of 3-amino-5-fluoro-benzonitrile. Example **122** was obtained as a white solid (10 mg). LCMS ($M+H^+$): 379. ^1H NMR (400MHz, CD_3OD) δ ppm 8.57 (s, 1H),

7.77 (s, 1H), 7.55 (dd, *J*=2.8, 6.3 Hz, 1H), 7.52 - 7.47 (m, 1H), 7.44 - 7.39 (m, 1H), 7.18 (t, *J*=8.8 Hz, 2H), 7.08 (t, *J*=9.0 Hz, 1H), 4.97 (s, 2H), 4.31 (t, *J*=5.5 Hz, 2H), 4.09 (t, *J*=5.4 Hz, 2H), 3.76 (s, 1H).

Example 123:

N-(3-chloro-5-fluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

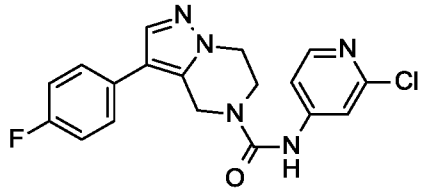


Preparation of Example 123:

The title compound was prepared in analogy to the preparation of Example **106** by using 3-chloro-5-fluoro-aniline instead of 3-amino-5-fluoro-benzonitrile. Example **123** was obtained as a white solid (9 mg). LCMS ($M+H^+$): 389. ^{1}H NMR (400MHz, CD_3OD) δ ppm 7.77 (s, 1H), 7.53 - 7.45 (m, 2H), 7.35 (d, *J*=0.9 Hz, 1H), 7.28 (td, *J*=2.1, 11.2 Hz, 1H), 7.22 - 7.14 (m, 2H), 6.84 (td, *J*=2.0, 8.5 Hz, 1H), 4.98 (s, 2H), 4.31 (t, *J*=5.4 Hz, 2H), 4.09 (t, *J*=5.5 Hz, 2H).

Example 124:

N-(2-chloro-4-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

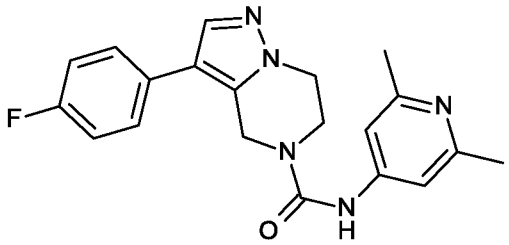


Preparation of Example 124:

The title compound was prepared in analogy to the preparation of Example **106** by using 2-chloropyridin-4-amine instead of 3-amino-5-fluoro-benzonitrile. Example **124** was obtained as a white solid (10 mg). LCMS ($M+H^+$): 372. ^{1}H NMR (400MHz, CD_3OD) δ ppm 8.15 (d, *J*=5.9 Hz, 1H), 7.77 (s, 1H), 7.69 (d, *J*=1.9 Hz, 1H), 7.53 - 7.43 (m, 3H), 7.19 (t, *J*=8.8 Hz, 2H), 5.00 (s, 2H), 4.32 (t, *J*=5.4 Hz, 2H), 4.11 (t, *J*=5.4 Hz, 2H).

Example 125:

N-(2,6-dimethyl-4-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

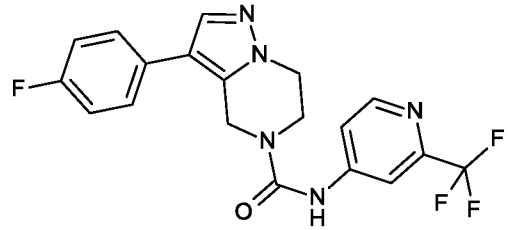


Preparation of Example 125:

The title compound was prepared in analogy to the preparation of Example **106** by using 2,6-dimethylpyridin-4-amine instead of 3-amino-5-fluoro-benzonitrile. Example **125** was obtained as a white solid (10 mg). LCMS ($M+H^+$): 366. ^{1}H NMR (400MHz, CD_3OD) δ ppm 7.77 (s, 1H), 7.48 (dd, *J*=5.3, 8.8 Hz, 2H), 7.41 (s, 2H), 7.18 (t, *J*=8.8 Hz, 2H), 5.00 (s, 2H), 4.32 (t, *J*=5.5 Hz, 2H), 4.11 (t, *J*=5.5 Hz, 2H), 2.52 (s, 6H).

Example 126:

3-(4-fluorophenyl)-N-[2-(trifluoromethyl)-4-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

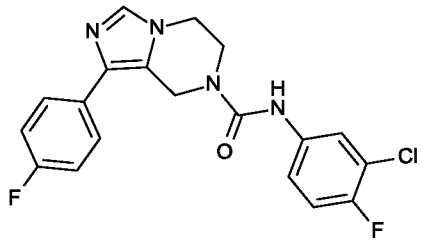


Preparation of Example 126:

The title compound was prepared in analogy to the preparation of Example **106** by using 2-(trifluoromethyl)pyridin-4-amine instead of 3-amino-5-fluoro-benzonitrile. Example **126** was obtained as a white solid (9 mg). LCMS ($M+H^+$): 406. ^{1}H NMR (400MHz, CD_3OD) δ ppm 8.48 (d, *J*=5.8 Hz, 1H), 8.02 (d, *J*=2.0 Hz, 1H), 7.77 (s, 1H), 7.74 (dd, *J*=2.0, 5.6 Hz, 1H), 7.49 (dd, *J*=5.3, 8.8 Hz, 2H), 7.26 - 7.13 (m, 2H), 5.02 (s, 2H), 4.36 - 4.32 (t, *J*=5.5 Hz, 2H), 4.13 (t, *J*=5.5 Hz, 2H).

Example 127:

N-(3-chloro-4-fluoro-phenyl)-1-(4-fluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide

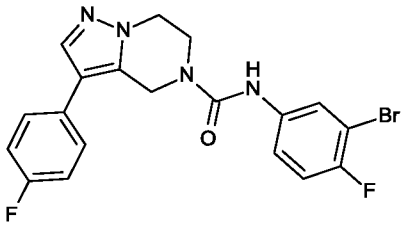


Preparation of Example 127:

The title compound was prepared in analogy to the preparation of Example **106** by using 3-chloro-4-fluoroaniline instead of 3-amino-5-fluoro-benzonitrile and 1-(4-fluorophenyl)-5,6,7,8-tetrahydroimidazo[1,5-a]pyrazine (compound **9e**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **127** was obtained as a white solid (21 mg). LCMS ($M+H^+$): 389. ^1H NMR (400MHz, CD_3OD) δ ppm 7.76 (s, 1H), 7.69 - 7.59 (m, 3H), 7.35 - 7.31 (m, 1H), 7.23 - 7.11 (m, 3H), 4.99 (s, 2H), 4.27 (t, *J*=5.4 Hz, 2H), 3.99 (t, *J*=5.4 Hz, 2H).

Example 128:

N-(3-bromo-4-fluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

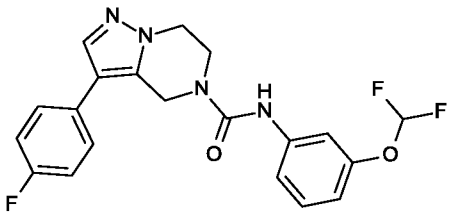


Preparation of Example 128:

The title compound was prepared in analogy to the preparation of Example **106** by using 3-bromo-4-fluoro-aniline instead of 3-amino-5-fluoro-benzonitrile. Example **128** was obtained as a white solid (3 mg). LCMS ($M+H^+$): 433. ^1H NMR (400MHz, CD_3OD) δ ppm 7.80 - 7.70 (m, 2H), 7.49 (dd, *J*=5.3, 9.0 Hz, 2H), 7.39 - 7.35 (m, 1H), 7.23 - 7.08 (m, 3H), 4.97 (s, 2H), 4.31 (t, *J*=5.5 Hz, 2H), 4.08 (t, *J*=5.4 Hz, 2H).

Example 129:

N-[3-(difluoromethoxy)phenyl]-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

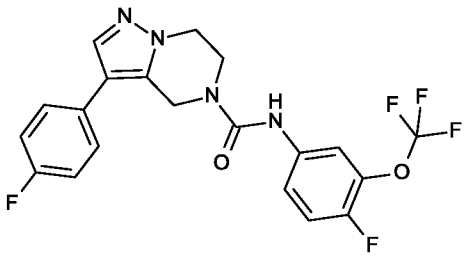


Preparation of Example 129:

The title compound was prepared in analogy to the preparation of Example **106** by using 3-(difluoromethoxy)aniline instead of 3-amino-5-fluoro-benzonitrile. Example **129** was obtained as a white solid (6 mg). LCMS ($M+H^+$): 403. ^1H NMR (400MHz, CD_3OD) δ ppm 7.77 (s, 1H), 7.49 (dd, *J*=5.3, 8.8 Hz, 2H), 7.36 - 7.22 (m, 3H), 7.18 (t, *J*=8.8 Hz, 2H), 6.80 (t, *J*=76 Hz, 1H), 6.83 (d, *J*=7.8 Hz, 1H), 4.98 (s, 2H), 4.31 (t, *J*=5.4 Hz, 2H), 4.10 (t, *J*=5.5 Hz, 2H).

Example 130:

3-(4-fluorophenyl)-N-[4-fluoro-3-(trifluoromethoxy)phenyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

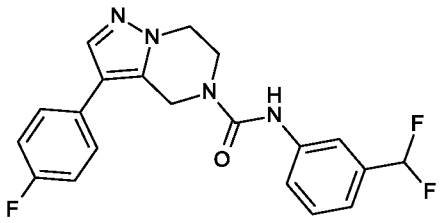


Preparation of Example 130:

The title compound was prepared in analogy to the preparation of Example **106** by using 4-fluoro-3-(trifluoromethoxy)aniline instead of 3-amino-5-fluoro-benzonitrile. Example **130** was obtained as a white solid (6 mg). LCMS ($M+H^+$): 439. ^1H NMR (400MHz, CD_3OD) δ ppm 7.77 (s, 1H), 7.62 (dd, *J*=1.1, 6.9 Hz, 1H), 7.53 - 7.46 (m, 2H), 7.42 - 7.38 (m, 1H), 7.29 - 7.11 (m, 3H), 4.98 (s, 2H), 4.31 (t, *J*=5.4 Hz, 2H), 4.09 (t, *J*=5.5 Hz, 2H).

Example 131:

N-[3-(difluoromethyl)phenyl]-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

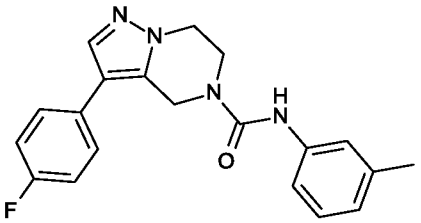


Preparation of Example 131:

The title compound was prepared in analogy to the preparation of Example **106** by using 3-(difluoromethyl)aniline instead of 3-amino-5-fluoro-benzonitrile. Example **131** was obtained as a white solid (12 mg). LCMS ($M+H^+$): 387. ^1H NMR (400MHz, CD_3OD) δ ppm 7.77 (s, 1H), 7.65 (s, 1H), 7.59 - 7.45 (m, 3H), 7.41 (t, *J*=7.9 Hz, 1H), 7.24 - 7.13 (m, 3H), 6.73 (t, *J*=56 Hz, 1H), 4.99 (s, 2H), 4.32 (t, *J*=5.4 Hz, 2H), 4.11 (t, *J*=5.4 Hz, 2H).

Example 132:

3-(4-fluorophenyl)-N-(m-tolyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

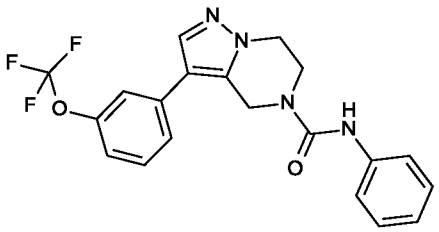


Preparation of Example 132:

The title compound was prepared in analogy to the preparation of Example **106** by using 3-methylaniline instead of 3-amino-5-fluoro-benzonitrile. Example **132** was obtained as a white solid (5 mg). LCMS ($M+H^+$): 351. ^1H NMR (400MHz, CD_3OD) δ ppm 7.77 (s, 1H), 7.49 (dd, *J*=5.3, 8.5 Hz, 2H), 7.27 - 7.08 (m, 5H), 6.90 (d, *J*=3.8 Hz, 1H), 4.97 (s, 2H), 4.31 (t, *J*=5.4 Hz, 2H), 4.09 (t, *J*=5.4 Hz, 2H), 2.32 (s, 3H).

Example 133:

N-phenyl-3-[3-(trifluoromethoxy)phenyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

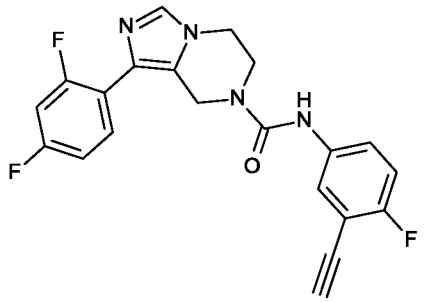


Preparation of Example 133:

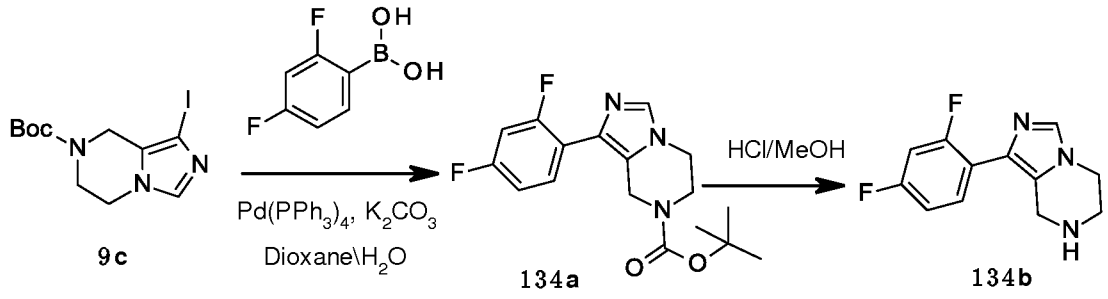
The title compound was prepared in analogy to the preparation of Example **1** by using 3-(trifluoromethoxy)phenyl-boronic acid instead of (4-fluorophenyl)boronic acid. Example **133** was obtained as a white solid (21 mg). LCMS ($M+H^+$): 403. ^1H NMR (400MHz, CD_3OD) δ ppm 7.86 (s, 1H), 7.58 - 7.44 (m, 2H), 7.42 - 7.36 (m, 3H), 7.29 (t, *J*=7.9 Hz, 2H), 7.21 (d, *J*=8.0 Hz, 1H), 7.11 - 7.02 (m, 1H), 5.02 (s, 2H), 4.33 (t, *J*=5.4 Hz, 2H), 4.11 (t, *J*=5.4 Hz, 2H).

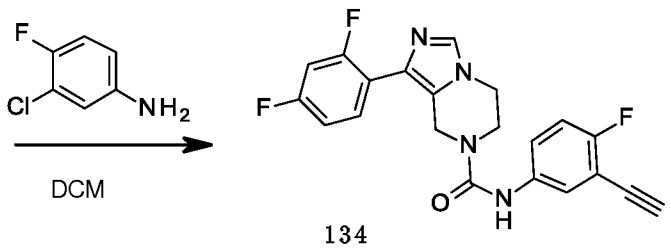
Example 134:

1-(2,4-difluorophenyl)-N-(3-ethynyl-4-fluoro-phenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide



The title compound was prepared according to the following scheme:





Preparation of 1-(2,4-difluorophenyl)-5,6,7,8-tetrahydroimidazo[1,5-a]pyrazine (compound 134b):

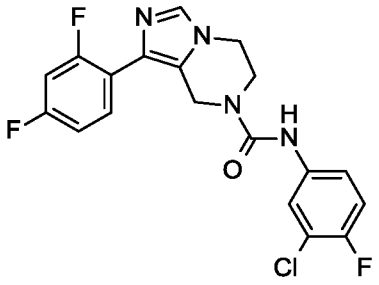
The compound **134b** was prepared in analogy to compound **9e** by using (2,4-difluorophenyl)boronic acid instead of (4-fluorophenyl)boronic acid. Compound **134b** was obtained as a white solid (250 mg). LCMS ($M+H^+$): 236.

Preparation of 1-(2,4-difluorophenyl)-N-(3-ethynyl-4-fluoro-phenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide (Example 134):

The title compound was prepared in analogy to the preparation of Example **106** by using 3-ethynyl-4-fluoro-aniline instead of 3-amino-5-fluoro-benzonitrile and 1-(2,4-difluorophenyl)-5,6,7,8-tetrahydroimidazo[1,5-a]pyrazine (compound **134b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **134** was obtained as a white solid (11 mg). LCMS ($M+H^+$): 397. ^{1}H NMR (400MHz, CD_3OD) δ ppm 7.81 (s, 1H), 7.70 - 7.59 (m, 1H), 7.53 (dd, *J*=2.8, 6.3 Hz, 1H), 7.41 – 7.37 (m, 1H), 7.15 - 7.01 (m, 3H), 4.81 (s, 2H), 4.28 (t, *J*=5.5 Hz, 2H), 3.99 (*J*=5.5 Hz, 2H), 3.75 (s, 1H).

Example 135:

N-(3-chloro-4-fluoro-phenyl)-1-(2,4-difluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide

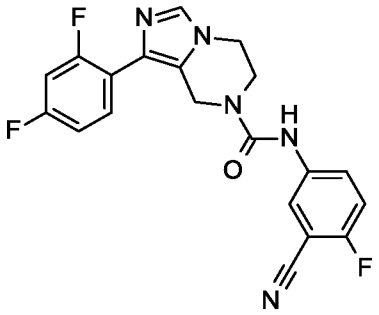


Preparation of Example 135:

The title compound was prepared in analogy to the preparation of Example **106** by using 3-chloro-4-fluoro-aniline instead of 3-amino-5-fluoro-benzonitrile and 1-(2,4-difluorophenyl)-5,6,7,8-tetrahydroimidazo[1,5-a]pyrazine (compound **134b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **135** was obtained as a white solid (18 mg). LCMS ($M+H^+$): 407. ^{1}H NMR (400MHz, CD_3OD) δ ppm 7.82 (s, 1H), 7.69 - 7.56 (m, 2H), 7.32 - 7.28 (m, 1H), 7.20 - 7.00 (m, 3H), 4.81 (d, *J*=1.0 Hz, 2H), 4.28 (t, *J*=5.4 Hz, 2H), 3.99 (*J*=5.5 Hz, 2H).

Example 136:

N-(3-cyano-4-fluoro-phenyl)-1-(2,4-difluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide

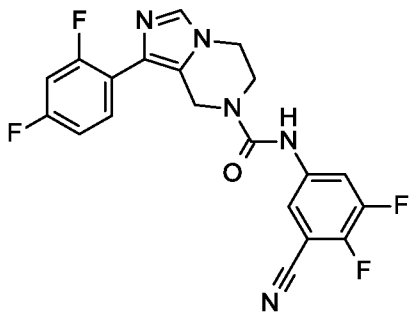


Preparation of Example 136:

The title compound was prepared in analogy to the preparation of Example **106** by using 5-amino-2-fluoro-benzonitrile instead of 3-amino-5-fluoro-benzonitrile and 1-(2,4-difluorophenyl)-5,6,7,8-tetrahydroimidazo[1,5-a]pyrazine (compound **134b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **136** was obtained as a white solid (23 mg). LCMS ($M+H^+$): 398. ^{1}H NMR (400MHz, CD_3OD) δ ppm 7.87 - 7.76 (m, 2H), 7.74 - 7.58 (m, 2H), 7.28 (t, *J*=9.0 Hz, 1H), 7.15 - 7.04 (m, 2H), 4.82 (d, *J*=1.0 Hz, 2H), 4.29 (t, *J*=5.5 Hz, 2H), 4.00 (t, *J*=5.5 Hz, 2H).

Example 137:

N-(3-cyano-4,5-difluoro-phenyl)-1-(2,4-difluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide



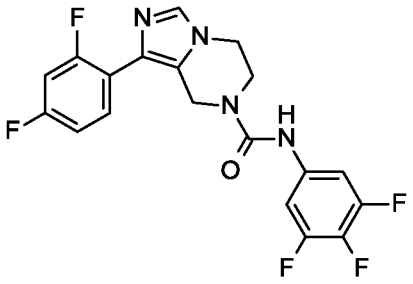
Preparation of Example 137:

The title compound was prepared in analogy to the preparation of Example **106** by using 5-amino-2,3-difluoro-benzonitrile instead of 3-amino-5-fluoro-benzonitrile and 1-(2,4-difluorophenyl)-5,6,7,8-tetrahydroimidazo[1,5-a]pyrazine (compound **134b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **137** was obtained as a white solid (8 mg). LCMS ($M+H^+$): 416. ^{1}H NMR (400MHz, CD_3OD) δ ppm 7.83

(s, 1H), 7.70 - 7.53 (m, 2H), 7.29 - 7.25 (m, 1H), 7.13 - 7.02 (m, 2H), 4.85 (d, *J*=1.0 Hz, 2H), 4.32 (t, *J*=5.4 Hz, 2H), 4.03 (t, *J*=5.4 Hz, 2H).

Example 138:

1-(2,4-difluorophenyl)-N-(3,4,5-trifluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide

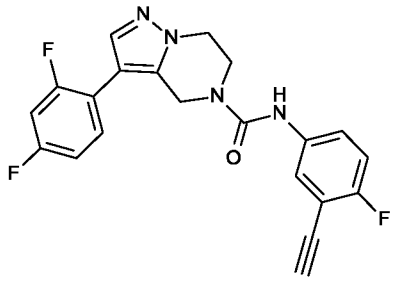


Preparation of Example 138:

The title compound was prepared in analogy to the preparation of Example **106** by using 3,4,5-trifluoroaniline instead of 3-amino-5-fluoro-benzonitrile and 1-(2,4-difluorophenyl)-5,6,7,8-tetrahydroimidazo[1,5-a]pyrazine (compound **134b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **138** was obtained as a white solid (10 mg). LCMS ($M+H^+$): 409. ^1H NMR (400MHz, CD_3OD) δ ppm 7.82 (s, 1H), 7.64 (dt, *J*=6.5, 8.7 Hz, 1H), 7.30 - 7.17 (m, 2H), 7.14 - 7.02 (m, 2H), 4.80 (d, *J*=1.0 Hz, 2H), 4.28 (t, *J*=5.4 Hz, 2H), 3.98 (t, *J*=5.4 Hz, 2H).

Example 139:

3-(2,4-difluorophenyl)-N-(3-ethynyl-4-fluoro-phenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



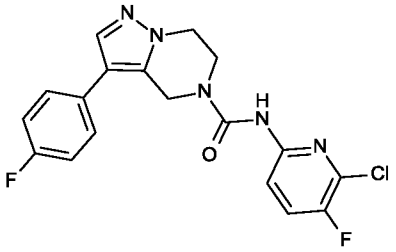
Preparation of Example 139:

The title compound was prepared in analogy to the preparation of Example **106** by using 3-ethynyl-4-fluoro-aniline instead of 3-amino-5-fluoro-benzonitrile and 3-(2,4-difluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **60b**) instead of 3-(4-fluorophenyl)-

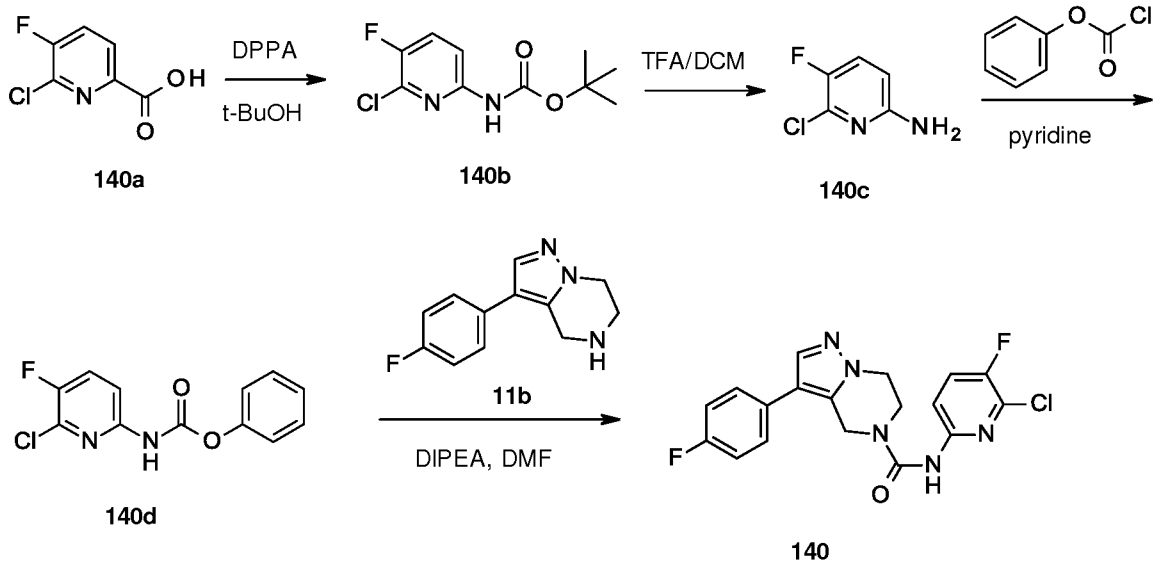
4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **70** was obtained as a white solid (9 mg). LCMS ($M+H^+$): 397. ^1H NMR (400MHz, CD_3OD) δ ppm 7.72 (d, *J*=1.5 Hz, 1H), 7.57 - 7.44 (m, 2H), 7.42 - 7.38 (m, 1H), 7.17 - 6.99 (m, 3H), 4.86 (s, 2H), 4.32 (t, *J*=5.5 Hz, 2H), 4.09 (t, *J*=5.5 Hz, 2H), 3.76 (s, 1H).

Example 140:

N-(6-chloro-5-fluoro-2-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: preparation of tert-butyl N-(6-chloro-5-fluoro-2-pyridyl)carbamate (compound 140b)

To a solution of 6-chloro-5-fluoro-pyridine-2-carboxylic acid (compound **140a**, 1.8 g, 10 mmol) and Et_3N (1.4 mL, 10 mmol) in tert-butanol (40 mL) was added diphenylphosphoryl azide (2.1 mL, 10 mmol) and the reaction mixture was stirred at 85 °C for 2 hours. Then the reaction mixture was concentrated and the residue was purified by column chromatography (eluting with 5%~30% EtOAc in petroleum ether) to afford compound **140b** (1.5 g) as a slight yellow oil. LCMS ($M+H^+$): 247.

Step 2: preparation of 6-chloro-5-fluoro-pyridin-2-amine (compound 140c)

A solution of tert-butyl N-(6-chloro-5-fluoro-2-pyridyl)carbamate (compound **140b**, 1.5 g, 6 mmol) in TFA/DCM (10 mL, 1:1, v/v) was stirred at room temperature for 2 hours. The reaction mixture was concentrated, the residue was diluted with EtOAc (30 mL), washed with saturated aqueous $NaHCO_3$ (50 mL) and brine (500 mL). The organic layer was dried over Na_2SO_4 and concentrated to afford compound **140c** (880 mg) which was used directly in next step.

Step 3: preparation of phenyl N-(6-chloro-5-fluoro-2-pyridyl)carbamate (compound 140d)

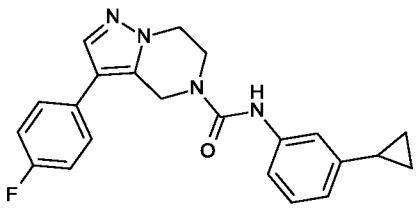
To a solution of 6-chloro-5-fluoro-pyridin-2-amine (compound **140c**, 880 mg, 6 mmol) and Pyridine (2 mL) in THF/DCM (10 mL, 1:1, v/v) was added phenyl carbonochloridate (1.4 g, 9 mmol) slowly at 0 °C. The resulting mixture was stirred at room temperature for 2 hours, then poured into water (20 mL) and extracted with EtOAc (20 mL) twice. The organic layers were combined and concentrated, the residue was purified by column chromatography (eluting with 5%~30% EtOAc in petroleum ether) to afford compound **140d** (800 mg) as a white solid. LCMS ($M+H^+$): 267.

Step 4: preparation of N-(6-chloro-5-fluoro-2-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 140):

A mixture of phenyl N-(6-chloro-5-fluoro-2-pyridyl)carbamate (compound **140d**, 27 mg, 0.1 mmol), 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**, 22 mg, 0.1 mmol) and DIPEA (65 mg, 0.5 mmol) in DMF (2 mL) was stirred at 70 °C for 1 hour. Then the reaction mixture was purified by prep-HPLC to afford Example **140** as a white solid. LCMS ($M+H^+$): 390. ^1H NMR (400MHz, CD_3OD) δ ppm 7.83 (dd, *J*=3.1, 8.9 Hz, 1H), 7.77 (s, 1H), 7.65 (dd, *J*=8.0, 8.8 Hz, 1H), 7.49 (dd, *J*=5.3, 8.8 Hz, 2H), 7.17 (t, *J*=8.9 Hz, 2H), 4.98 (s, 2H), 4.30 (t, *J*=5.4 Hz, 2H), 4.09 (t, *J*=5.4 Hz, 2H).

Example 141:

N-(3-cyclopropylphenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

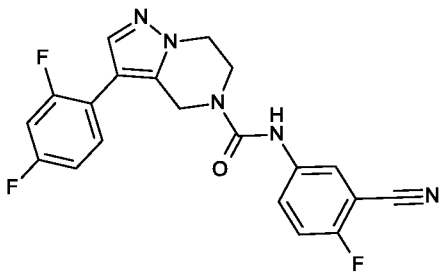


Preparation of Example 141:

The title compound was prepared in analogy to the preparation of Example **106** by using 3-cyclopropylaniline (CAS: 485402-64-0, catalog number: AQ14074, Shanghai AQBioPharma Co. Ltd) instead of 3-amino-5-fluoro-benzonitrile. Example **141** was obtained as a white solid (6 mg). LCMS ($M+H^+$): 377. ^1H NMR (400MHz, CD_3OD) δ ppm 7.77 (s, 1H), 7.49 (dd, *J*=5.3, 8.8 Hz, 2H), 7.25 - 7.04 (m, 5H), 6.87 - 6.73 (m, 1H), 4.97 (s, 2H), 4.31 (t, *J*=5.4 Hz, 2H), 4.09 (t, *J*=5.4 Hz, 2H), 1.96 - 1.79 (m, 1H), 1.00 - 0.90 (m, 2H), 0.74 - 0.60 (m, 2H).

Example 142:

N-(3-cyano-4-fluoro-phenyl)-3-(2,4-difluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

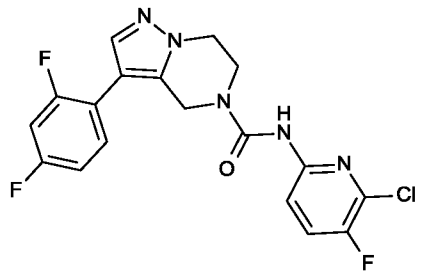


Preparation of Example 142:

The title compound was prepared in analogy to the preparation of Example **106** by using 5-amino-2-fluoro-benzonitrile instead of 3-amino-5-fluoro-benzonitrile and 3-(2,4-difluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **50b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **142** was obtained as a white solid (4 mg). LCMS ($M+H^+$): 398. ^1H NMR (400MHz, CD_3OD) δ ppm 7.87 - 7.77 (m, 1H), 7.75 - 7.65 (m, 2H), 7.54 - 7.40 (m, 1H), 7.29 (t, *J*=8.9 Hz, 1H), 7.15 - 7.01 (m, 2H), 4.87 (s, 2H), 4.33 (t, *J*=5.4 Hz, 2H), 4.11 (t, *J*=5.5 Hz, 2H).

Example 143:

N-(6-chloro-5-fluoro-2-pyridyl)-3-(2,4-difluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

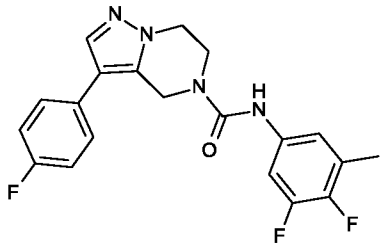


Preparation of Example 143:

The title compound was prepared in analogy to the preparation of Example **140** by using 3-(2,4-difluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **60b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **143** was obtained as a white solid. LCMS ($M+H^+$): 408. ^1H NMR (400MHz, CD_3OD) δ ppm 7.81 (dd, *J*=3.0, 8.8 Hz, 1H), 7.71 (d, *J*=1.3 Hz, 1H), 7.64 (t, *J*=8.4 Hz, 1H), 7.54 - 7.42 (m, 1H), 7.14 - 7.02 (m, 2H), 4.87 (s, 2H), 4.32 (t, *J*=5.5 Hz, 2H), 4.12 (t, *J*=5.5 Hz, 2H).

Example 144:

N-(3,4-difluoro-5-methyl-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

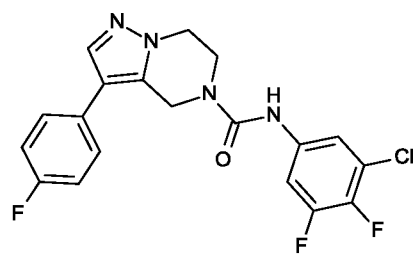


Preparation of Example 144:

The title compound was prepared in analogy to the preparation of Example **106** by using 3,4-difluoro-5-methyl-aniline (CAS: 1505944-46-6, catalog number: AQ14079, Shanghai AQBioPharma Co. Ltd) instead of 3-amino-5-fluoro-benzonitrile. Example **144** was obtained as a white solid (10 mg). LCMS ($M+H^+$): 387. ^1H NMR (400MHz, DMSO-d_6) δ ppm 8.99 (s, 1H), 7.83 (s, 1H), 7.49 (dd, *J*=5.4, 8.9 Hz, 2H), 7.44 - 7.38 (m, 1H), 7.32 - 7.22 (m, 2H), 7.11 (d, *J*=6.0 Hz, 1H), 4.92 (s, 2H), 4.21 (t, *J*=5.4 Hz, 2H), 3.99 (t, *J*=5.4 Hz, 2H), 2.24 (d, *J*=2.0 Hz, 3H).

Example 145:

N-(3-chloro-4,5-difluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

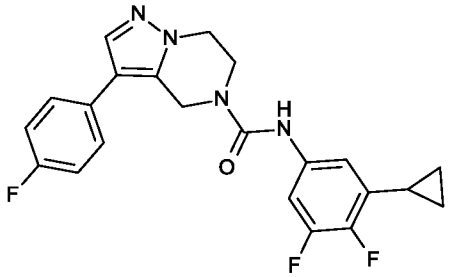


Preparation of Example 145:

The title compound was prepared in analogy to the preparation of Example **106** by using 3-chloro-4,5-difluoro-aniline (CAS: 149144-05-8, catalog number: AQ14076, Shanghai AQBioPharma Co. Ltd) instead of 3-amino-5-fluoro-benzonitrile. Example **145** was obtained as a white solid (10 mg). LCMS ($M+H^+$): 407. ^1H NMR (400MHz, CD_3OD) δ ppm 7.77 (s, 1H), 7.50 - 7.35 (m, 4H), 7.18 (t, *J*=8.8 Hz, 2H), 4.97 (s, 2H), 4.31 (t, *J*=5.4 Hz, 2H), 4.08 (t, *J*=5.4 Hz, 2H).

Example 146:

N-(3-cyclopropyl-4,5-difluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

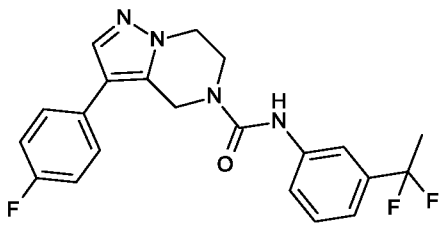


Preparation of Example 146:

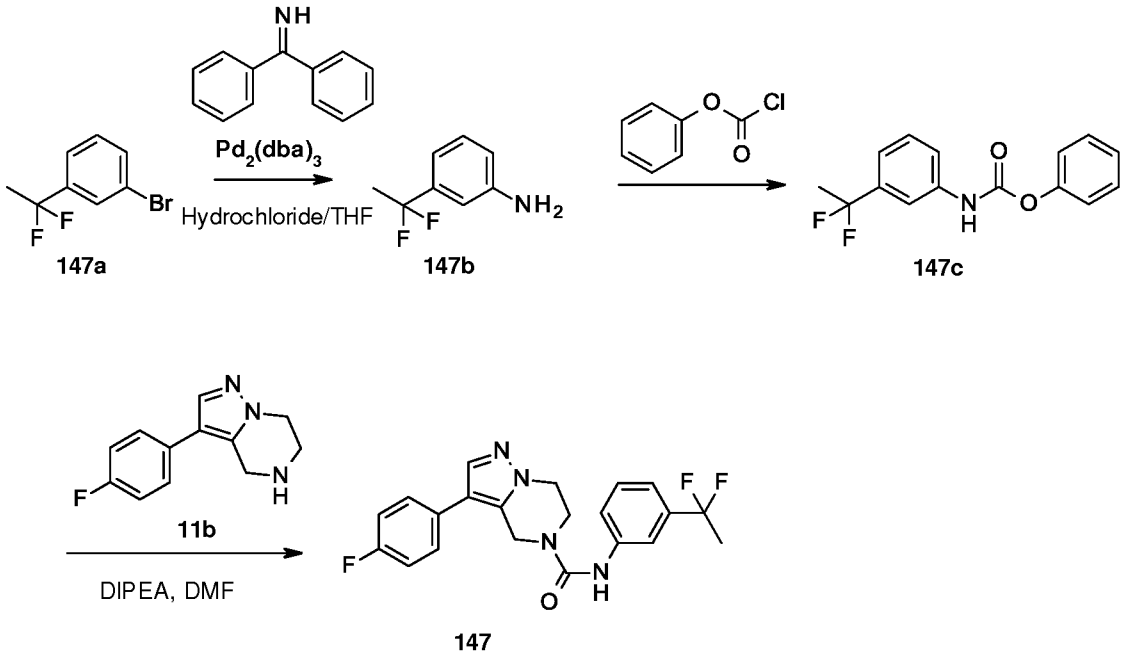
The title compound was prepared in analogy to the preparation of Example **106** by using 3-cyclopropyl-4,5-difluoro-aniline (catalog number: AQ14078, Shanghai AQBioPharma Co. Ltd) instead of 3-amino-5-fluoro-benzonitrile. Example **146** was obtained as a white solid (10 mg). LCMS ($M+H^+$): 413. ^1H NMR (400MHz, CD_3OD) δ ppm 7.77 (s, 1H), 7.48 (dd, *J*=5.3, 8.8 Hz, 2H), 7.29 - 7.12 (m, 3H), 6.79 - 6.69 (m, 1H), 4.95 (s, 2H), 4.30 (t, *J*=5.5 Hz, 2H), 4.07 (t, *J*=5.5 Hz, 2H), 2.16 - 2.03 (m, 1H), 1.09 - 0.98 (m, 2H), 0.80 - 0.68 (m, 2H).

Example 147:

N-[3-(1,1-difluoroethyl)phenyl]-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: **preparation of 3-(1,1-difluoroethyl)aniline (compound147b):**

To a mixture of 1-bromo-3-(1,1-difluoroethyl)benzene (compound **147a**, 440 mg, 2 mmol)), diphenylmethanimine (545 mg, 3 mmol), 2-Dicyclohexylphosphino-2',6'-dimethoxy-1,1'-biphenyl (164 mg, 0.4 mmol) and Cs_2CO_3 (1.4 g, 4 mmol) in toluene (20 mL) was added $Pd_2(dba)_3$ (163 mg, 0.2 mmol) under nitrogen. The reaction mixture was stirred at 110 °C for 16 hours under nitrogen. After cooled down to room temperature, the reaction mixture was washed with brine (20 mL) and the organic layer was concentrated. The residue was dissolved in THF (10 mL) and hydrochloride acid (2 mL, 12 M). The reaction mixture was stirred at room temperature for 2 hours and then diluted with EtOAc and petroleum ether (20 mL, 1:1, v/v), washed with Hydrochloride acid (20 mL, 2 M). The aqueous layer was neutralized to pH ~7 and extracted with EtOAc (20 mL) twice. The organic layer was dried and concentrated to afford compound **147b** (158 mg) as a slight yellow oil. LCMS ($M+H^+$): 158.

Step 2: preparation of phenyl N-[3-(1,1-difluoroethyl)phenyl]carbamate (compound147c):

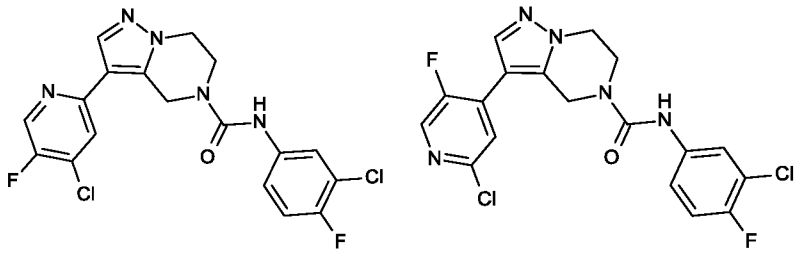
To a solution of 3-(1,1-difluoroethyl)aniline (compound **147b**, 158 mg, 1 mmol) and Pyridine (0.5 mL) in THF/DCM (5 mL, 1:1, v/v) was added phenyl carbonochloridate (234 mg, 1.5 mmol) slowly at 0 °C. The resulting mixture was stirred at room temperature for 2 hours, poured into water (20 mL) and extracted with EtOAc (20 mL) twice. The organic layer was combined and concentrated, the residue was purified by column chromatography (eluting with 0%~20% EtOAc in petroleum ether) to afford compound **147c** (80 mg) as a white solid. LCMS ($M+H^+$): 278.

Step 3: preparation of N-[3-(1,1-difluoroethyl)phenyl]-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 147):

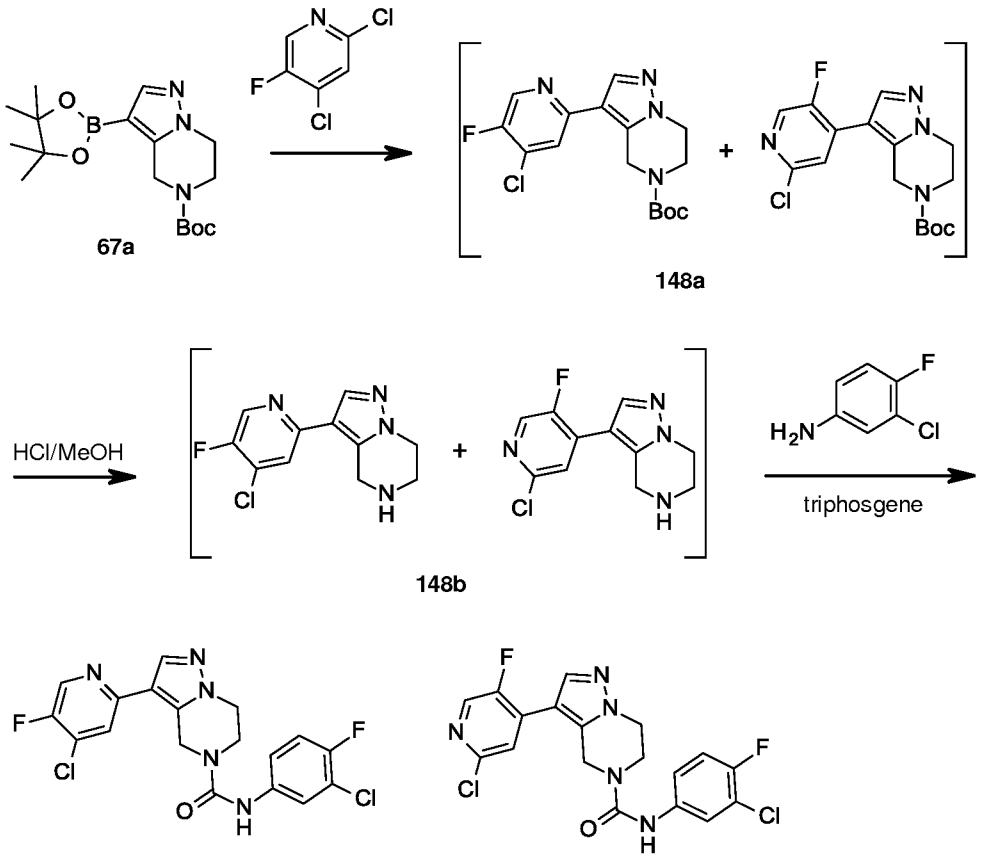
The title compound was prepared in analogy to the preparation of Example **140** by using N-[3-(1,1-difluoroethyl)phenyl]carbamate (compound **147c**) instead of N-(6-chloro-5-fluoro-2-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (compound **140d**). Example **147** was obtained as a white solid (4 mg). LCMS ($M+H^+$): 401. ^1H NMR (400MHz, CD_3OD) δ ppm 7.77 (s, 1H), 7.63 (s, 1H), 7.50 (dd, *J*=5.3, 8.8 Hz, 2H), 7.38 (t, *J*=7.9 Hz, 1H), 7.26 - 7.13 (m, 4H), 4.99 (s, 2H), 4.32 (t, *J*=5.5 Hz, 2H), 4.11 (t, *J*=5.5 Hz, 2H), 1.91 (t, *J*=18.2 Hz, 3H).

Example 148 and Example 149:

N-(3-chloro-4-fluoro-phenyl)-3-(4-chloro-5-fluoro-2-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide and **N-(3-chloro-4-fluoro-phenyl)-3-(2-chloro-5-fluoro-4-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide**



The title compound was prepared according to the following scheme:



Preparation of [3-(4-chloro-5-fluoro-2-pyridyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine and 3-(2-chloro-5-fluoro-4-pyridyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine] (compound 148b):

The compound **148b** was prepared in analogy to compound **67c** by using 2,4-dichloro-5-fluoro-pyridine instead of 2-chloro-4-(trifluoromethyl)pyridine. Compound **148b** was obtained as a white solid (50 mg). LCMS ($M+H^+$): 253.

Preparation of N-(3-chloro-4-fluoro-phenyl)-3-(4-chloro-5-fluoro-2-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide and **N-(3-chloro-4-fluoro-phenyl)-3-(2-chloro-5-fluoro-4-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 148 and 149):**

The title compound was prepared in analogy to the preparation of Example **140** by using phenyl N-(3-chloro-4-fluoro-phenyl)carbamate (compound **12i**) instead of phenyl N-(6-chloro-5-fluoro-2-pyridyl)carbamate (compound **140d**) and compound **148b** instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**).

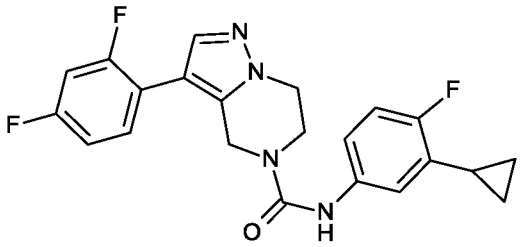
Example **148** (2 mg) was obtained as a white solid. LCMS ($M+H^+$): 424. ^{1}H NMR (400MHz, CD_3OD) δ ppm 8.36 (d, *J*=2.3 Hz, 1H), 7.96 (d, *J*=2.5 Hz, 1H), 7.61 (dd, *J*=2.5, 6.8

Hz, 1H), 7.58 (d, *J*=5.5 Hz, 1H), 7.34 - 7.30 (m, 1H), 7.17 (t, *J*=9.0 Hz, 1H), 5.00 (s, 2H), 4.34 (t, *J*=5.4 Hz, 2H), 4.11 (t, *J*=5.5 Hz, 2H).

Example **149** (18 mg) was obtained as a white solid. LCMS ($M+H^+$): 424. ^1H NMR (400MHz, CD_3OD) δ ppm 8.55 (d, *J*=1.3 Hz, 1H), 8.07 (s, 1H), 7.90 (d, *J*=5.8 Hz, 1H), 7.62 (dd, *J*=2.6, 6.7 Hz, 1H), 7.36 - 7.31 (m, 1H), 7.17 (t, *J*=9.0 Hz, 1H), 5.16 (s, 2H), 4.31 (t, *J*=5.4 Hz, 2H), 4.06 (t, *J*=5.5 Hz, 2H).

Example 150

N-(3-cyclopropyl-4-fluoro-phenyl)-3-(2,4-difluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

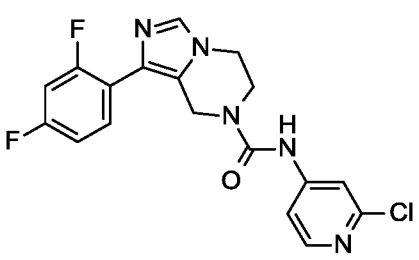


Preparation of Example 150:

The title compound was prepared in analogy to the preparation of Example **106** by using 3-cyclopropyl-4-fluoro-aniline (CAS: 890129-90-5, catalog number: AQ14079, Shanghai AQBioPharma Co. Ltd) instead of 3-amino-5-fluoro-benzonitrile and 3-(2,4-difluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **60b**, 40 mg) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **150** was obtained as a white solid (13 mg). LCMS ($M+H^+$): 413. ^1H NMR (400MHz, chloroform-d) δ ppm 7.68 (s, 1H), 7.38 - 7.27 (m, 1H), 7.10 - 6.86 (m, 5H), 6.57 (br. s, 1H), 4.74 (s, 2H), 4.36 (br. s, 2H), 4.04 (br. s, 2H), 2.09 – 2.03 (m, 1H), 1.04 - 0.91 (m, 2H), 0.77 - 0.63 (m, 2H).

Example 151:

N-(2-chloro-4-pyridyl)-1-(2,4-difluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide

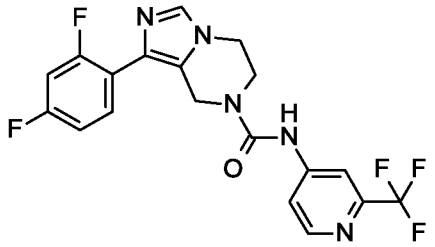


Preparation of Example 151:

The title compound was prepared in analogy to the preparation of Example **106** by using 2-chloro-pyridin-4-amine instead of 3-amino-5-fluoro-benzonitrile and 1-(2,4-difluorophenyl)-5,6,7,8-tetrahydroimidazo[1,5-a]pyrazine (compound **134b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **151** was obtained as a white solid (2 mg). LCMS ($M+H^+$): 390. ^1H NMR (400MHz, CD_3OD) δ ppm 8.13 (d, *J*=5.8 Hz, 1H), 7.82 (s, 1H), 7.70 - 7.59 (m, 2H), 7.44 (dd, *J*=2.0, 5.8 Hz, 1H), 7.16 - 7.02 (m, 2H), 4.83 (s, 2H), 4.30 (t, *J*=5.5 Hz, 2H), 4.01 (t, *J*=5.5 Hz, 2H).

Example 152:

1-(2,4-difluorophenyl)-N-[2-(trifluoromethyl)-4-pyridyl]-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide

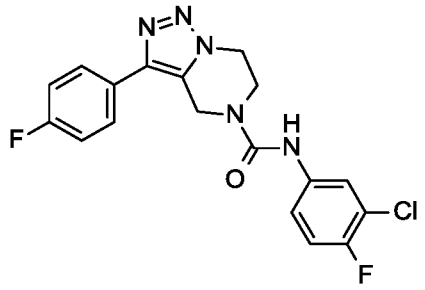


Preparation of Example 152:

The title compound was prepared in analogy to the preparation of Example **106** by using 2-(trifluoromethyl)pyridine-4-amine instead of 3-amino-5-fluoro-benzonitrile and 1-(2,4-difluorophenyl)-5,6,7,8-tetrahydroimidazo[1,5-a]pyrazine (compound **134b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **152** was obtained as a white solid (2 mg). LCMS ($M+H^+$): 424. ^1H NMR (400MHz, CD_3OD) δ ppm 7.99 (s, 1H), 7.78 (s, 1H), 7.75 (d, *J*=1.3 Hz, 1H), 7.54 - 7.45 (m, 2H), 7.41 (dd, *J*=1.9, 8.9 Hz, 1H), 7.18 (t, *J*=8.8 Hz, 1H), 5.01 (s, 2H), 4.33 (t, *J*=5.5 Hz, 2H), 4.12 (t, *J*=5.4 Hz, 2H).

Example 153:

N-(3-chloro-4-fluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-triazolo[1,5-a]pyrazine-5-carboxamide

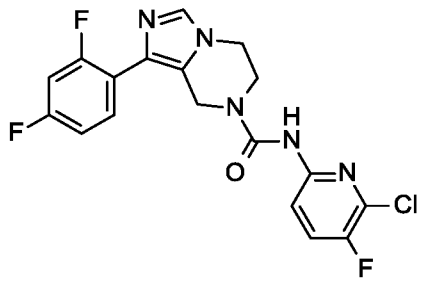


Preparation of Example 153:

The title compound was prepared in analogy to the preparation of Example **140** by using phenyl N-(3-chloro-4-fluoro-phenyl)carbamate (compound **12i**) instead of phenyl N-(6-chloro-5-fluoro-2-pyridyl)carbamate (compound **140d**) and 3-(4-fluorophenyl)-4,5,6,7-tetrahydrotriazolo[1,5-a]pyrazine (compound **10e**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **153** was obtained as a white solid (5 mg). LCMS ($M+H^+$): 390. ^{1}H NMR (400MHz, CD_3OD) δ ppm 7.85 - 7.75 (m, 2H), 7.64 (dd, *J*=2.6, 6.7 Hz, 1H), 7.37 - 7.33 (m, 1H), 7.27 (t, *J*=8.8 Hz, 2H), 7.18 (t, *J*=9.0 Hz, 1H), 5.09 (s, 2H), 4.58 (t, *J*=5.4 Hz, 2H), 4.11 ((t, *J*=5.4 Hz, 2H).

Example 154:

N-(6-chloro-5-fluoro-2-pyridyl)-1-(2,4-difluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide

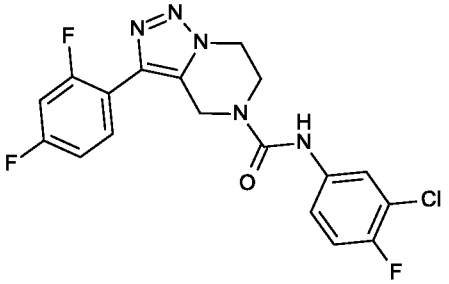


Preparation of Example 154:

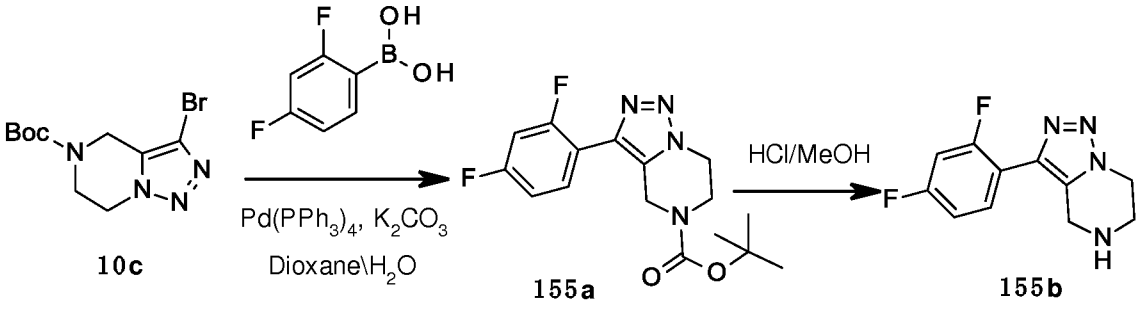
The title compound was prepared in analogy to the preparation of Example **140** by using 1-(2,4-difluorophenyl)-5,6,7,8-tetrahydroimidazo[1,5-a]pyrazine (compound **134b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **154** was obtained as a white solid (5 mg). LCMS ($M+H^+$): 408. ^{1}H NMR (400MHz, CD_3OD) δ ppm 7.84 - 7.77 (m, 2H), 7.69 - 7.59 (m, 2H), 7.15 - 7.01 (m, 2H), 4.82 (d, *J*=0.8 Hz, 2H), 4.29 (t, *J*=5.5 Hz, 2H), 4.00 (t, *J*=5.5 Hz, 2H).

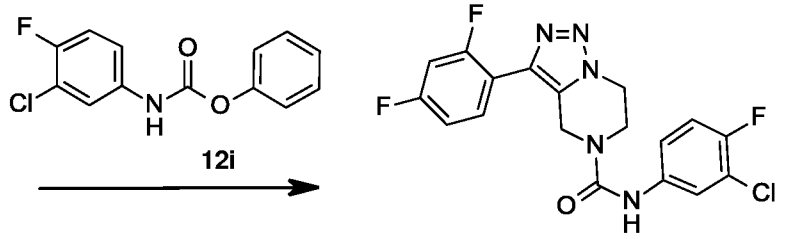
Example 155:

N-(3-chloro-4-fluoro-phenyl)-3-(2,4-difluorophenyl)-6,7-dihydro-4H-triazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:





Preparation of 3-(2,4-difluorophenyl)-4,5,6,7-tetrahydrotriazolo[1,5-a]pyrazine (compound 155b):

The compound **155b** was prepared in analogy to compound **10e** by using (2,4-difluorophenyl)boronic acid instead of (4-fluorophenyl)boronic acid. Compound **155b** was obtained as a white solid (50 mg). LCMS ($M+H^+$): 237.

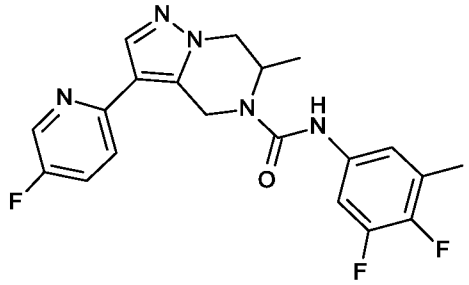
Preparation of N-(3-chloro-4-fluoro-phenyl)-3-(2,4-difluorophenyl)-6,7-dihydro-4H-triazolo[1,5-a]pyrazine-5-carboxamide (Example 155):

The title compound was prepared in analogy to the preparation of Example **140** by using phenyl N-(3-chloro-4-fluoro-phenyl)carbamate (compound **12i**) instead of phenyl N-(6-chloro-5-fluoro-2-pyridyl)carbamate (compound **140d**) and 3-(2,4-difluorophenyl)-4,5,6,7-tetrahydrotriazolo[1,5-a]pyrazine (compound **155b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **155** was obtained as a white solid

(7 mg). LCMS ($M+H^+$): 408. ^1H NMR (400MHz, CD_3OD) δ ppm 7.80 (dt, *J*=6.5, 8.8 Hz, 1H), 7.61 (dd, *J*=2.6, 6.7 Hz, 1H), 7.35 - 7.27 (m, 1H), 7.23 - 7.11 (m, 3H), 4.94 (s, 2H), 4.60 (t, *J*=5.5 Hz, 2H), 4.13 (t, *J*=5.5 Hz, 2H).

Example 156:

N-(3,4-difluoro-5-methyl-phenyl)-3-(5-fluoro-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

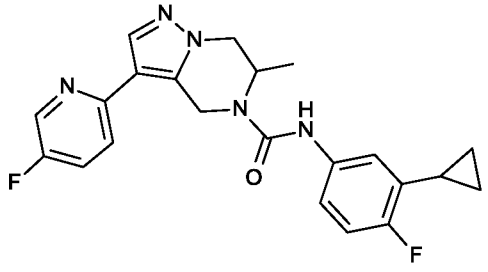


Preparation of Example 156:

The title compound was prepared in analogy to the preparation of Example **106** by using 3,4-difluoro-5-methyl-aniline (CAS: 1505944-46-6, catalog number: AQ14079, Shanghai AQBioPharma Co. Ltd) instead of 3-amino-5-fluoro-benzonitrile and 3-(5-fluoro-2-pyridyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **94b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **156** was obtained as a white solid (8 mg). LCMS ($M+H^+$): 402. ^1H NMR (400MHz, CD_3OD) δ ppm 8.50 (d, *J*=3.0 Hz, 1H), 8.06 (s, 1H), 7.75 (dd, *J*=4.1, 8.9 Hz, 1H), 7.61 (dt, *J*=3.0, 8.7 Hz, 1H), 7.30-7.26 (m, 1H), 7.10 - 6.96 (m, 1H), 5.46 (d, *J*=18.1 Hz, 1H), 5.04 - 4.94 (m, 1H), 4.83 (d, *J*=17.8 Hz, 1H), 4.37 (dd, *J*=4.5, 12.8 Hz, 1H), 4.29 - 4.17 (m, 1H), 2.30 (d, *J*=2.3 Hz, 3H), 1.29 (d, *J*=6.8 Hz, 3H).

Example 157:

N-(3-cyclopropyl-4-fluoro-phenyl)-3-(5-fluoro-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

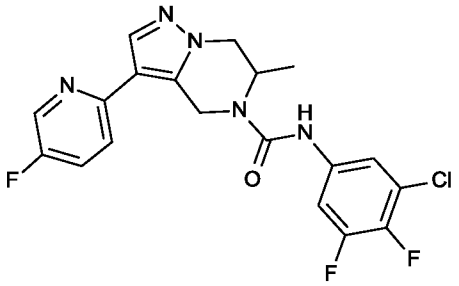


Preparation of Example 157:

The title compound was prepared in analogy to the preparation of Example **106** by using 3-cyclopropyl-4-fluoro-aniline instead of 3-amino-5-fluoro-benzonitrile and 3-(5-fluoro-2-pyridyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **94b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **157** was obtained as a white solid (9 mg). LCMS ($M+H^+$): 410. ^1H NMR (400MHz, CD_3OD) δ ppm 8.50 (d, *J*=3.0 Hz, 1H), 8.06 (s, 1H), 7.74 (dd, *J*=4.3, 8.8 Hz, 1H), 7.61 (dt, *J*=3.0, 8.7 Hz, 1H), 7.19 - 7.15 (m, 1H), 7.06 - 6.92 (m, 2H), 5.46 (d, *J*=17.8 Hz, 1H), 5.06 - 4.96 (m, 1H), 4.82 (d, *J*=18.1 Hz, 1H), 4.37 (dd, *J*=4.3, 12.5 Hz, 1H), 4.22 (d, *J*=12.3 Hz, 1H), 2.18 - 2.01 (m, 1H), 1.28 (d, *J*=7.0 Hz, 3H), 1.04 - 0.92 (m, 2H), 0.81 - 0.67 (m, 2H).

Example 158:

N-(3-chloro-4,5-difluoro-phenyl)-3-(5-fluoro-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

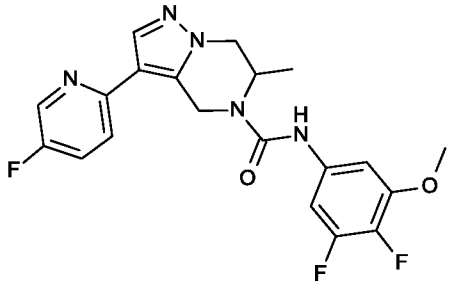


Preparation of Example 158:

The title compound was prepared in analogy to the preparation of Example **106** by using 3-chloro-4,5-difluoro-aniline (CAS: 149144-05-8, catalog number: AQ14076, Shanghai AQBioPharma Co. Ltd) instead of 3-amino-5-fluoro-benzonitrile and 3-(5-fluoro-2-pyridyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **94b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **158** was obtained as a white solid (11 mg). LCMS ($M+H^+$): 422. ^1H NMR (400MHz, CD_3OD) δ ppm 8.51 (d, *J*=3.0 Hz, 1H), 8.06 (s, 1H), 7.75 (dd, *J*=4.4, 8.9 Hz, 1H), 7.61 (dt, *J*=3.0, 8.7 Hz, 1H), 7.51 - 7.40 (m, 2H), 5.47 (d, *J*=17.8 Hz, 1H), 5.05 - 4.97 (m, 1H), 4.84 (d, *J*=18.1 Hz, 1H), 4.38 (dd, *J*=4.6, 12.9 Hz, 1H), 4.23 (d, *J*=12.5 Hz, 1H), 1.29 (d, *J*=6.8 Hz, 3H).

Example 159:

N-(3,4-difluoro-5-methoxy-phenyl)-3-(5-fluoro-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

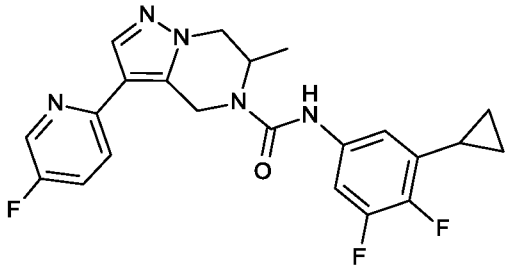


Preparation of Example 159:

The title compound was prepared in analogy to the preparation of Example **106** by using 3,4-difluoro-5-methoxyl-aniline (CAS: 1195190-12-5, catalog number: AQ12805, Shanghai AQBioPharma Co. Ltd) instead of 3-amino-5-fluoro-benzonitrile and 3-(5-fluoro-2-pyridyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **94b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **159** was obtained as a white solid (5 mg). LCMS ($M+H^+$): 418. ^1H NMR (400MHz, CD_3OD) δ ppm 8.51 (d, *J*=3.0 Hz, 1H), 8.07 (s, 1H), 7.75 (dd, *J*=4.3, 8.8 Hz, 1H), 7.61 (dt, *J*=2.9, 8.6 Hz, 1H), 7.10 - 6.97 (m, 2H), 5.48 (d, *J*=17.8 Hz, 1H), 5.05 - 4.99 (m, 1H), 4.84 (d, *J*=18.1 Hz, 1H), 4.38 (dd, *J*=4.4, 12.9 Hz, 1H), 4.23 (d, *J*=13.3 Hz, 1H), 3.90 (s, 3H), 1.30 (d, *J*=7.0 Hz, 3H).

Example 160:

N-(3-cyclopropyl-4,5-difluoro-phenyl)-3-(5-fluoro-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



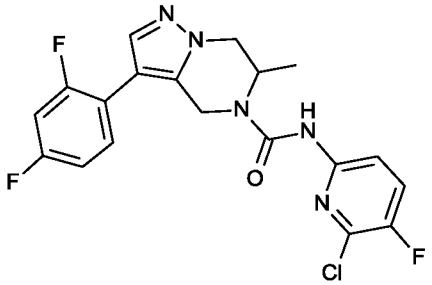
Preparation of Example 160:

The title compound was prepared in analogy to the preparation of Example **106** by using 3-cyclopropyl-4,5-difluoro-aniline (catalog number: AQ14078, Shanghai AQBioPharma Co. Ltd) instead of 3-amino-5-fluoro-benzonitrile and 3-(5-fluoro-2-pyridyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **94b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **160** was obtained as a white solid (8 mg). LCMS ($M+H^+$): 428. ^1H NMR (400MHz, CD_3OD) δ ppm 8.50 (d, *J*=3.0 Hz, 1H), 8.06 (s, 1H), 7.75 (dd, *J*=4.1, 8.9 Hz, 1H), 7.61 (dt, *J*=3.0, 8.7 Hz, 1H), 7.27 - 7.23 (m, 1H), 6.83 - 6.72

(m, 1H), 5.46 (d, *J*=18.1 Hz, 1H), 5.04 - 4.96 (m, 1H), 4.82 (d, *J*=17.8 Hz, 2H), 4.37 (dd, *J*=4.5, 12.8 Hz, 1H), 4.22 (d, *J*=13.1 Hz, 1H), 2.18 - 2.07 (m, 1H), 1.28 (d, *J*=6.8 Hz, 3H), 1.12 - 0.97 (m, 2H), 0.84 - 0.69 (m, 2H).

Example 161:

N-(6-chloro-5-fluoro-2-pyridyl)-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

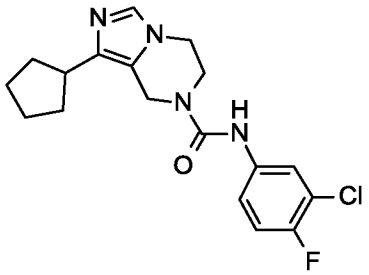


Preparation of Example 161:

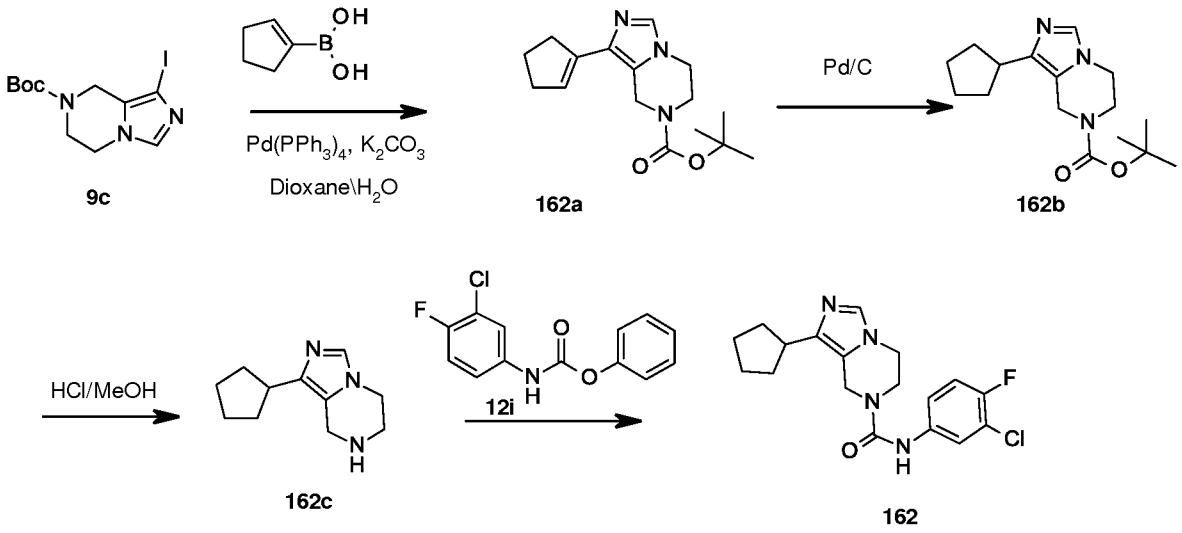
The title compound was prepared in analogy to the preparation of Example **140** by using 3-(2,4-difluorophenyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **85b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **161** was afforded as a white solid (5 mg). LCMS ($M+H^+$): 422. ^{1}H NMR (400MHz, CD_3OD) δ ppm 7.83 (dd, *J*=3.0, 8.8 Hz, 1H), 7.75 (d, *J*=1.8 Hz, 1H), 7.66 (dd, *J*=7.8, 8.8 Hz, 1H), 7.57 - 7.47 (m, 1H), 7.17 - 7.03 (m, 2H), 5.15 (d, *J*=16.8 Hz, 1H), 5.05 - 4.99 (m, 1H), 4.61 (d, *J*=16.8 Hz, 1H), 4.39 (dd, *J*=4.3, 12.8 Hz, 1H), 4.24 (d, *J*=12.8 Hz, 1H), 1.30 (d, *J*=7.0 Hz, 3H).

Example 162:

N-(3-chloro-4-fluoro-phenyl)-1-cyclopentyl-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide



The title compound was prepared according to the following scheme:



Preparation of 1-cyclopentyl-5,6,7,8-tetrahydroimidazo[1,5-a]pyrazine (compound 162c):

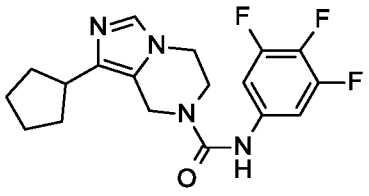
The compound **162c** was prepared in analogy to compound **26c** by using tert-butyl 1-iodo-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxylate (compound **9c**) instead of tert-butyl 3-iodo-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **1e**). Compound **162c** was obtained as a slight yellow solid (40 mg). LCMS ($M+H^+$): 192.

Preparation of N-(3-chloro-4-fluoro-phenyl)-1-cyclopentyl-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide (Example 162):

The title compound was prepared in analogy to the preparation of Example **140** by using phenyl N-(3-chloro-4-fluoro-phenyl)carbamate (compound **12i**) instead of phenyl N-(6-chloro-5-fluoro-2-pyridyl)carbamate (compound **140d**) and 1-cyclopentyl-5,6,7,8-tetrahydroimidazo[1,5-a]pyrazine (compound **162c**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **162** was obtained as a white solid (37 mg). LCMS ($M+H^+$): 363. ^1H NMR (400MHz, CD_3OD) δ ppm 7.70 (s, 1H), 7.63 (dd, *J*=2.5, 6.5 Hz, 1H), 7.39 - 7.29 (m, 1H), 7.17 (t, *J*=8.9 Hz, 1H), 4.77 (s, 2H), 4.18 (t, *J*=5.3 Hz, 2H), 3.92 (t, *J*=5.4 Hz, 2H), 3.07 - 2.92 (m, 1H), 2.06 - 1.92 (m, 2H), 1.90 - 1.78 (m, 2H), 1.77 - 1.64 (m, 4H).

Example 163:

1-cyclopentyl-N-(3,4,5-trifluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide

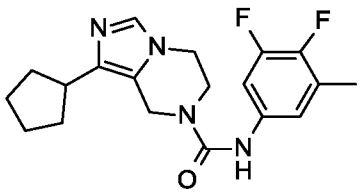


Preparation of Example 163:

The title compound was prepared in analogy to the preparation of Example **106** by using 3,4,5-trifluoroaniline instead of 3-amino-5-fluoro-benzonitrile and 1-cyclopentyl-5,6,7,8-tetrahydroimidazo[1,5-a]pyrazine (compound **162c**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **163** was obtained as a white solid (6 mg). LCMS ($M+H^+$): 365. ^{1}H NMR (400MHz, chloroform-d) δ ppm 8.31 (br. s, 1H), 7.90 (br. s, 1H), 7.35 - 7.28 (m, 2H), 4.74 (s, 2H), 4.33 (t, *J*=5.0 Hz, 2H), 4.03 (t, *J*=5.0 Hz, 2H), 3.03 - 2.95 (m, 1H), 2.09 - 1.96 (m, 2H), 1.90 - 1.58 (m, 6H).

Example 164:

1-cyclopentyl-N-(3,4-difluoro-5-methyl-phenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide

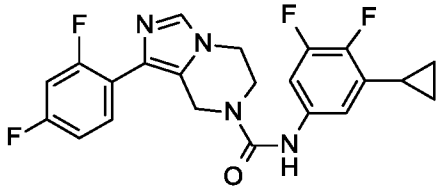


Preparation of Example 164:

The title compound was prepared in analogy to the preparation of Example **106** by using 3,4-difluoro-5-methyl-aniline (CAS: 1505944-46-6, catalog number: AQ14079, Shanghai AQBioPharma Co. Ltd) instead of 3-amino-5-fluoro-benzonitrile and 1-cyclopentyl-5,6,7,8-tetrahydroimidazo[1,5-a]pyrazine (compound **162c**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **164** was obtained as a white solid (9 mg). LCMS ($M+H^+$): 361. ^{1}H NMR (400MHz, chloroform-d) δ ppm 8.69 (br. s, 1H), 7.92 (br. s, 1H), 7.37 - 7.30 (m, 1H), 7.11 (d, *J*=5.5 Hz, 1H), 4.72 (s, 2H), 4.42 (br. s, 2H), 4.04 (br. s, 2H), 3.06 - 2.93 (m, 2H), 2.05 (d, *J*=8.9 Hz, 2H), 1.84 (d, *J*=6.1 Hz, 2H), 1.77 - 1.60 (m, 5H).

Example 165:

N-(3-cyclopropyl-4,5-difluoro-phenyl)-1-(2,4-difluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide

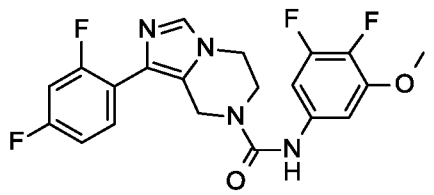


Preparation of Example 165:

The title compound was prepared in analogy to the preparation of Example **106** by using 3-cyclopropyl-4,5-difluoro-aniline (catalog number: AQ14078, Shanghai AQBioPharma Co. Ltd) instead of 3-amino-5-fluoro-benzonitrile and 1-(2,4-difluorophenyl)-5,6,7,8-tetrahydroimidazo[1,5-a]pyrazine (compound **134b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **165** was obtained as a white solid (15 mg). LCMS ($M+H^+$): 431. ^1H NMR (400MHz, chloroform-d) δ ppm 8.22 (br. s, 1H), 7.68 (br. s, 1H), 7.22 - 7.05 (m, 2H), 7.04 - 6.84 (m, 2H), 6.67 (br. s, 1H), 4.74 (br. s, 2H), 4.35 (br. s, 2H), 4.03 (br. s, 2H), 2.11 - 2.03 (m, 1H), 0.99 (d, *J*=8.3 Hz, 2H), 0.70 (d, *J*=5.3 Hz, 2H).

Example 166:

N-(3,4-difluoro-5-methoxy-phenyl)-1-(2,4-difluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide

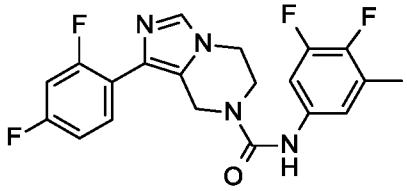


Preparation of Example 166:

The title compound was prepared in analogy to the preparation of Example **106** by using 3,4-difluoro-5-methoxyl-aniline (CAS: 1195190-12-5, catalog number: AQ12805, Shanghai AQBioPharma Co. Ltd) instead of 3-amino-5-fluoro-benzonitrile and 1-(2,4-difluorophenyl)-5,6,7,8-tetrahydroimidazo[1,5-a]pyrazine (compound **134b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **166** was obtained as a white solid (12 mg). LCMS ($M+H^+$): 421. ^1H NMR (400MHz, chloroform-d & CD_3OD) δ ppm 7.89 (s, 1H), 7.37 (dt, *J*=6.5, 8.5 Hz, 1H), 6.87 - 6.64 (m, 4H), 4.59 (s, 2H), 4.10 (t, *J*=5.3 Hz, 2H), 3.78 (t, *J*=5.3 Hz, 2H), 3.65 (s, 3H).

Example 167:

N-(3,4-difluoro-5-methyl-phenyl)-1-(2,4-difluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide

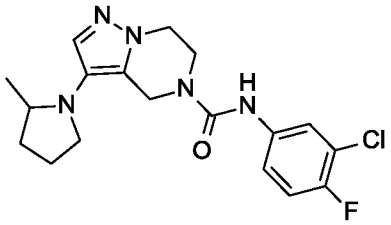


Preparation of Example 167:

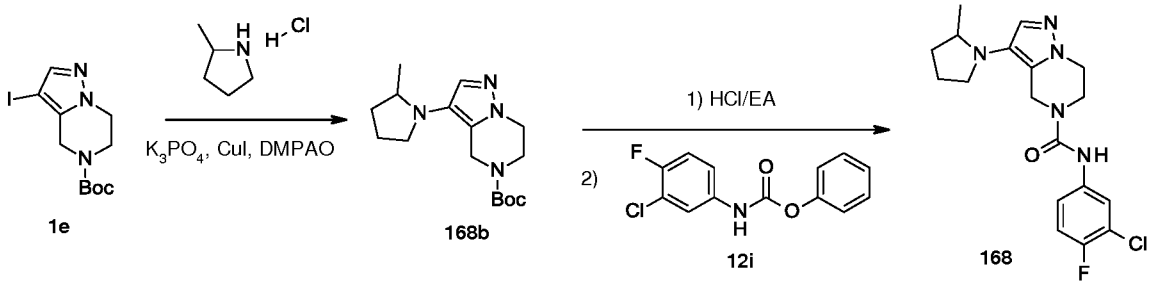
The title compound was prepared in analogy to the preparation of Example **106** by using 3,4-difluoro-5-methyl-aniline (CAS: 1505944-46-6, catalog number: AQ14079, Shanghai AQBioPharma Co. Ltd) instead of 3-amino-5-fluoro-benzonitrile and 1-(2,4-difluorophenyl)-5,6,7,8-tetrahydroimidazo[1,5-a]pyrazine (compound **134b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **167** was obtained ed as a white solid (11 mg). LCMS ($M+H^+$): 405. ^1H NMR (400MHz, chloroform-d) δ ppm 8.07 (br. s, 1H), 7.69 (br. s, 1H), 7.20 (t, *J*=7.0 Hz, 1H), 7.07 - 6.83 (m, 4H), 4.74 (br. s, 2H), 4.30 (br. s, 2H), 4.02 (br. s, 2H), 2.25 (s, 3H).

Example 168:

N-(3-chloro-4-fluoro-phenyl)-3-(2-methylpyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: **Preparation of tert-butyl 3-(2-methylpyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 168b)**

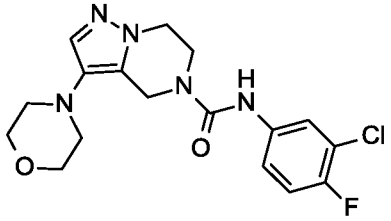
To a mixture of 3-iodo-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **1e**, 45 mg 0.13 mmol), K_3PO_4 (54 mg, 0.25 mmol), CuI (4.8 mg 25 μmol) and 2-(2,6-dimethylanilino)-2-oxo-acetic acid (DMPAO, 4.9 mg, 25 μmol) in DMSO (5.0 mL) was added 2-methylpyrrolidine hydrochloride (22 mg, 25 μmol). The reaction mixture was flushed with nitrogen and sealed. Then the reaction mixture was stirred at 100 °C in microwave for 2 hours. To the reaction mixture was added K_2CO_3 (35 mg, 0.25 mmol), and CuI (4.8 mg, 25 μmol). The reaction mixture was subjected to microwave at 120 °C for another 2 hours. The reaction mixture was diluted with ethyl acetate, washed with water. The organic layer was separated and concentrated. The residue was purified by column chromatography (eluting with 60%~70% EtOAc in petroleum ether) to give compound **168b** (12 mg). LCMS ($M+H^+$): 307.

Step 2: preparation of N-(3-chloro-4-fluoro-phenyl)-3-(2-methylpyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 168)

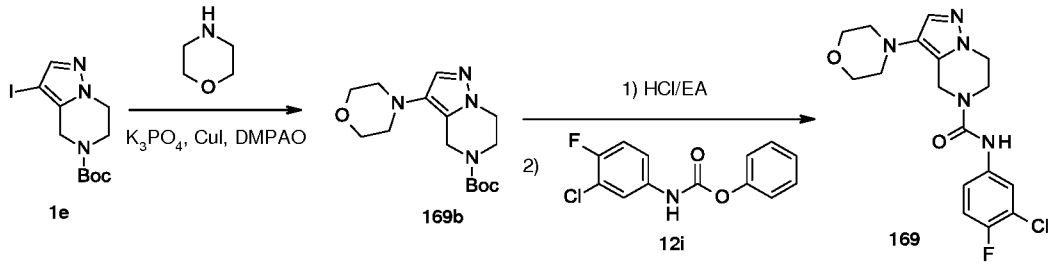
A solution of tert-butyl 3-(2-methylpyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **168b**, 31 mg, 0.1 mmol) in HCl/EA (1N, 5.0 mL) was stirred at room temperature overnight. Petroleum ether (45 mL) was added. The reaction mixture was centrifuged, and a yellowish solid was collected. The solid was dissolved in DCM (3.0 mL), to which was added DIPEA (0.1 mL) and phenyl N-(3-chloro-4-fluoro-phenyl)carbamate (32 mg, 0.3 mmol). The reaction mixture was stirred at 40 °C for 3 hours, and then concentrated in *vacuo* to give crude product, which was purified by preparative HPLC to afford Example **168** (10 mg). LCMS ($M+H^+$): 378. ^1H NMR (400MHz, chloroform-d) δ ppm 7.65 (dd, *J*=2.5, 6.5 Hz, 1H), 7.38 (s, 1H), 7.30 (br. s, 1H), 7.18 - 7.02 (m, 2H), 5.00 - 4.83 (m, 2H), 4.29 - 4.19 (m, 2H), 4.19 - 4.07 (m, 1H), 4.00 - 3.91 (m, 1H), 3.64 - 3.52 (m, 1H), 3.45 - 3.36 (m, 1H), 3.10 - 2.98 (m, 1H), 2.24 - 2.20 (m, 1H), 2.14 - 2.06 (m, 1H), 2.03 - 1.94 (m, 1H), 1.82 - 1.70 (m, 1H), 1.23 (d, *J*=6.0 Hz, 3H).

Example 169:

N-(3-chloro-4-fluoro-phenyl)-3-morpholino-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:

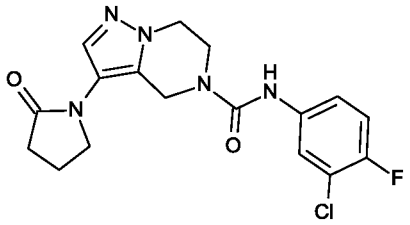


Preparation of N-(3-chloro-4-fluoro-phenyl)-3-(2-methylpyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 169):

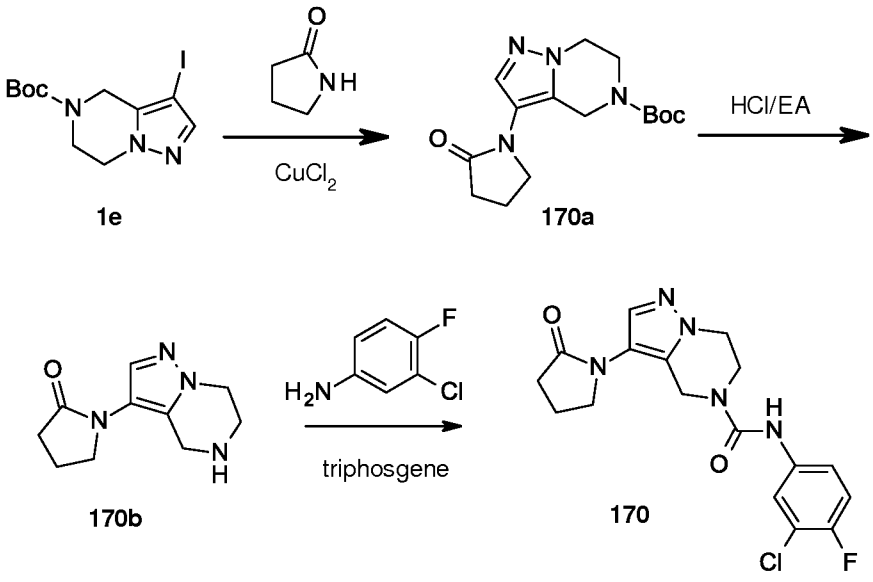
The title compound was prepared in analogy to Example **168** by using morpholine instead of 2-methylpyrrolidine hydrochloride. Example **169** was obtained as a slight yellow solid (15 mg). LCMS ($M+H^+$): 380. ^1H NMR (400MHz, chloroform-d) δ ppm 7.59 (dd, *J*=2.4, 6.4 Hz, 1H), 7.41 (s, 1H), 7.28 - 7.24 (m, 1H), 7.13 - 7.05 (m, 1H), 6.93 (br. s, 1H), 4.80 (s, 2H), 4.31 - 4.21 (m, 2H), 4.02 (d, *J*=5.0 Hz, 2H), 3.96 - 3.89 (m, 4H), 3.08 - 2.97 (m, 4H).

Example 170:

N-(3-chloro-4-fluoro-phenyl)-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: preparation of tert-butyl 3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 170a)

An oven-dried resealable Schlenk tube was charged with $CuCl_2$ (13.5 mg, 0.1 mmol), K_3PO_4 (424.5 mg, 2.0 mmol), tert-butyl 3-iodo-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **1e**, 350 mg, 1 mmol), pyrrolidin-2-one (102 mg, 1.2 mmol), (1R,2R)-N1,N2-dimethylcyclohexane-1,2-diamine (14.2 mg, 0.1 mmol) and dioxane (2 mL). The tube was flushed with N_2 and sealed. The reaction mixture was stirred at 110 °C for 23 hours. The reaction mixture was concentrated and the residue was purified by prep-TLC to afford compound **170a** (80.0 mg) as white solid.

Step 2: preparation of 1-(4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)pyrrolidin-2-one (compound 170b)

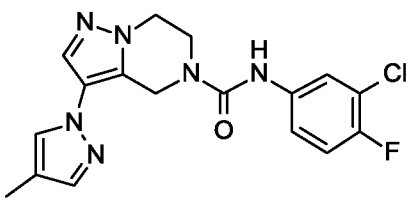
A solution of tert-butyl 3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **170a**, 40.0 mg) in HCl/EtOAc (5 mL) was stirred at room temperature for 2 hours. Then the reaction mixture was concentrated in *vacuo* to afford compound **170b** (30 mg) in HCl salt as a white solid.

Step 3: preparation of N-(3-chloro-4-fluoro-phenyl)-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 170):

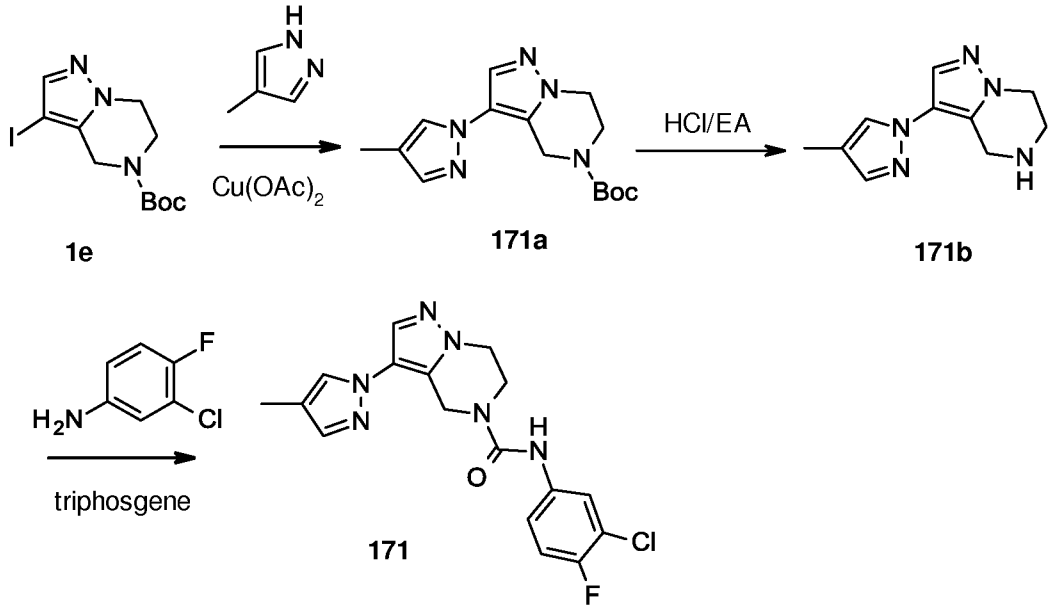
To a mixture of 3-chloro-4-fluoro-aniline (27 mg) and DIPEA (0.1 mL) in DCM (3 mL) was added triphosgene (25 mg). After stirring for 30 min at room temperature, 1-(4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)pyrrolidin-2-one (compound **170b**, 30 mg) was added. The resulting mixture was stirred at room temperature for 1 hour, then concentrated. The residue was purified by prep-HPLC to afford Example **170** (13 mg) as a white solid. LCMS ($M+H^+$): 378. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.02 (s, 1H), 7.73 (dd, *J*=2.6, 6.8 Hz, 1H), 7.57 (s, 1H), 7.45 - 7.39 (m, 1H), 7.35 - 7.29 (m, 1H), 4.68 (s, 2H), 4.17 - 4.14 (m, 2H), 3.97 - 3.93 (m, 2H), 3.73 (t, *J*=7.1 Hz, 2H), 2.44 - 2.38 (m, 2H), 2.10 (t, *J*=7.6 Hz, 2H).

Example 171:

N-(3-chloro-4-fluoro-phenyl)-3-(4-methylpyrazol-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: **preparation of tert-butyl 3-(4-methylpyrazol-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 171a):**

To a mixture of tert-butyl 3-iodo-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **1e**, 349 mg, 1.0 mmol), $Cu(AcO)_2$ (18 mg, 0.1 mmol) and Cs_2CO_3 (651 mg, 2.0 mmol) in DMF (2.0 mL) was added 4-methyl-1H-pyrazole (102 mg, 1.5 mmol), and the reaction mixture was stirred at 110 °C for 18 hours. The reaction mixture was filtered and the filtrate was purified by prep-HPLC to afford compound **171a** (50 mg).

Step 2: preparation of 3-(4-methylpyrazol-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine (compound 171b):

A mixture of tert-butyl 3-(4-methylpyrazol-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **171a**, 40 mg, 0.1 mmol) in HCl/EA (1N, 5.0 mL) was stirred at room temperature for 2 hours. The reaction mixture was concentrated to afford compound **171b** (40 mg).

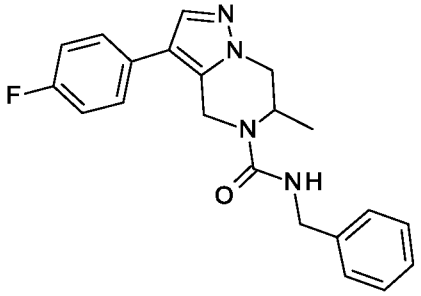
Step 3: preparation of N-(3-chloro-4-fluoro-phenyl)-3-(4-methylpyrazol-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 171):

To a mixture of 3-chloro-4-fluoro-aniline (29 mg, 0.2 mmol) and DIPEA (65 mg, 0.5 mmol) in DCM (3.0 mL) was added triphosgene (30 mg, 0.1 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 30 mins, then 3-(4-methylpyrazol-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine (compound **171b**, 40 mg) was added. The reaction mixture was stirred at room temperature for 1 hour. The reaction mixture was concentrated and the residue was purified by prep-HPLC to afford Example **171** (20.0 mg) as white solid. LCMS (M+1): 375. ^1H

NMR (400MHz, DMSO-d6) δ ppm 9.08 (s, 1H), 7.93 (s, 1H), 7.83 (s, 1H), 7.74 - 7.71 (m, 1H), 7.51 (s, 1H), 7.40 (dd, *J*=2.6, 4.3 Hz, 1H), 7.35 - 7.29 (m, 1H), 4.91 (s, 2H), 4.21 (t, *J*=5.2 Hz, 2H), 3.98 (t, *J*=5.3 Hz, 2H), 2.09 (s, 3H).

Example 172:

N-benzyl-3-(4-fluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

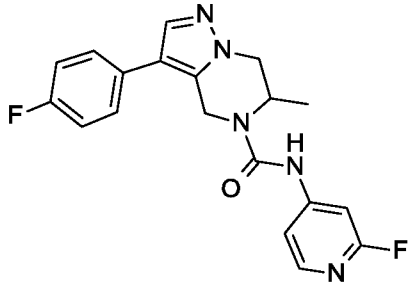


Preparation of Example 172:

The title compound was prepared in analogy to the preparation of Example **11** by using benzyl amine instead of 3-trifluoromethylaniline, and 3-(4-fluorophenyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **53f**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **172** was obtained as a white solid (18 mg). LCMS ($M+H^+$): 365. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 7.85 (s, 1H), 7.54 (dd, *J*=5.3, 8.8 Hz, 2H), 7.44 (s, 1H), 7.34 - 7.21 (m, 7H), 5.08 (d, *J*=16.7 Hz, 1H), 4.84 (d, *J*=5.1 Hz, 1H), 4.51 (d, *J*=16.7 Hz, 1H), 4.32 (t, *J*=6.6 Hz, 2H), 4.23 - 4.17 (m, 1H), 4.15 - 4.09 (m, 1H), 1.11 (d, *J*=6.9 Hz, 3H).

Example 173:

3-(4-fluorophenyl)-N-(2-fluoro-4-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

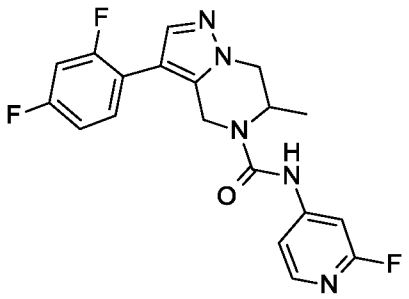


Preparation of Example 173:

The title compound was prepared in analogy to the preparation of Example **60** by using 2-fluoropyridin-4-amine instead of 5-fluoro-6-methyl-pyridin-2-amine and 3-(4-fluorophenyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **53f**) instead of 3-(2,4-difluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **60b**). Example **173** was obtained as a white solid (24 mg). LCMS ($M+H^+$): 370. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.50 (s, 1H), 8.03 (d, *J*=5.8 Hz, 1H), 7.87 (s, 1H), 7.55 (dd, *J*=5.5, 8.8 Hz, 2H), 7.37 (d, *J*=5.6 Hz, 1H), 7.32 - 7.24 (m, 3H), 5.23 (d, *J*=16.4 Hz, 1H), 4.94 (br. s, 1H), 4.70 (d, *J*=16.7 Hz, 1H), 4.32 - 4.25 (m, 1H), 4.23 - 4.16 (m, 1H), 1.20 (d, *J*=6.8 Hz, 3H).

Example 174:

3-(2,4-difluorophenyl)-N-(2-fluoro-4-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

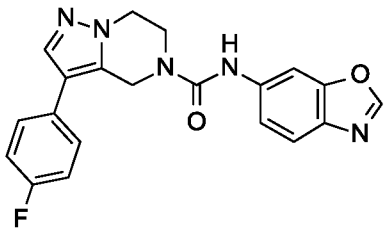


Preparation of Example 174:

The title compound was prepared in analogy to the preparation of Example **60** by using 2-fluoropyridin-4-amine instead of 5-fluoro-6-methyl-pyridin-2-amine and 3-(2,4-difluorophenyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **85b**) instead of 3-(2,4-difluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **60b**). Example **174** was obtained as a white solid (3 mg). LCMS ($M+H^+$): 388. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.42 (s, 1H), 8.01 (d, *J*=6.0 Hz, 1H), 7.74 (s, 1H), 7.56 (s, 1H), 7.37 (d, *J*=10.2 Hz, 2H), 7.28 (s, 1H), 7.21 (d, *J*=7.8 Hz, 1H), 5.10 (d, *J*=17.2 Hz, 1H), 4.94 (s, 1H), 4.56 (d, *J*=16.4 Hz, 1H), 4.31 - 4.23 (m, 1H), 4.04 (s, 1H), 1.21 (d, *J*=7.0 Hz, 3H).

Example 175:

N-(1,3-benzoxazol-6-yl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

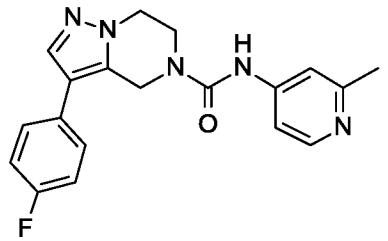


Preparation of Example 175:

The title compound was prepared in analogy to the preparation of Example **60** by using 1,3-benzoxazol-6-amine instead of 5-fluoro-6-methyl-pyridin-2-amine and 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**) instead of 3-(2,4-difluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **60b**). Example **175** was obtained as a white solid (11 mg). LCMS ($M+H^+$): 378. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.14 (s, 1H), 8.61 (s, 1H), 7.98 (d, *J*=1.6 Hz, 1H), 7.84 (s, 1H), 7.67 (d, *J*=8.5 Hz, 1H), 7.51 (dd, *J*=8.7, 5.4 Hz, 2H), 7.40 (dd, *J*=8.7, 1.9 Hz, 1H), 7.28 (t, *J*=8.8 Hz, 2H), 4.96 (s, 2H), 4.24 (t, *J*=5.2 Hz, 2H), 4.03 (t, *J*=5.1 Hz, 2H).

Example 176:

3-(4-fluorophenyl)-N-(2-methyl-4-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

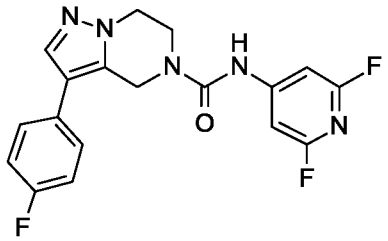


Preparation of Example 176:

The title compound was prepared in analogy to the preparation of Example **60** by using 2-methylpyridin-4-amine instead of 5-fluoro-6-methyl-pyridin-2-amine and 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**) instead of 3-(2,4-difluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **60b**). Example **176** was obtained as a white solid (5 mg). LCMS ($M+H^+$): 352. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 8.22 - 8.18 (m, 2H), 7.83 (s, 1H), 7.54 - 7.45 (m, 2H), 7.37 - 7.23 (m, 4H), 4.94 (s, 2H), 4.27 - 4.18 (m, 2H), 4.01 (t, *J*=5.4 Hz, 2H), 2.37 (s, 3H).

Example 177:

N-(2,6-difluoro-4-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

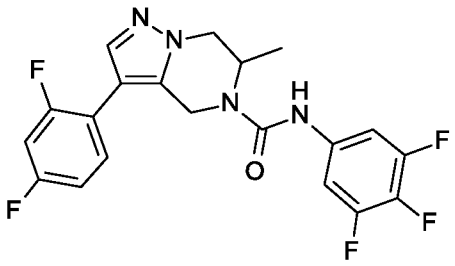


Preparation of Example 177:

The title compound was prepared in analogy to the preparation of Example **60** by using 2,6-difluoropyridin-4-amine instead of 5-fluoro-6-methyl-pyridin-2-amine and 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**) instead of 3-(2,4-difluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **60b**). Example **177** was obtained as a white solid (14 mg). LCMS ($M+H^+$): 374. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.92 (br. s, 1H), 7.84 (s, 1H), 7.49 (dd, *J*=5.5, 8.7 Hz, 2H), 7.28 (t, *J*=8.8 Hz, 2H), 7.16 (s, 2H), 4.97 (s, 2H), 4.25 (t, *J*=5.3 Hz, 2H), 4.03 (t, *J*=5.3 Hz, 2H).

Example 178:

3-(2,4-difluorophenyl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

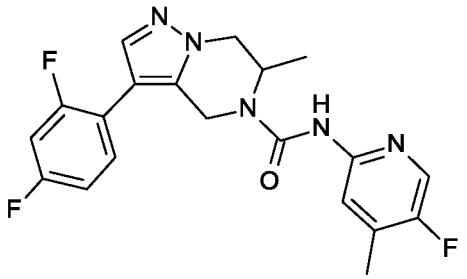


Preparation of Example 178:

The title compound was prepared in analogy to the preparation of Example **11** by using 3,4,5-trifluoroaniline instead of 3-(trifluoromethyl)aniline and 3-(2,4-difluorophenyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **85b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **178** was obtained as a white solid (5 mg). LCMS ($M+H^+$): 423. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.06 (s, 1H), 7.72 (d, *J*=1.9 Hz, 1H), 7.60 - 7.52 (m, 1H), 7.45 - 7.33 (m, 3H), 7.19 (dt, *J*=2.1, 8.5 Hz, 1H), 5.06 (d, J=16.8 Hz, 1H), 4.95 - 4.87 (m, 1H), 4.52 (d, *J*=16.9 Hz, 1H), 4.32 - 4.25 (m, 1H), 4.24 - 4.18 (m, 1H), 1.19 (d, J=6.8 Hz, 3H).

Example 179:

3-(2,4-difluorophenyl)-N-(5-fluoro-4-methyl-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

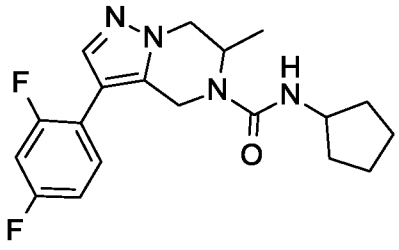


Preparation of Example 179:

The title compound was prepared in analogy to the preparation of Example **60** by using 5-fluoro-4-methyl-pyridin-2-amine instead of 3-(2,4-difluorophenyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **85b**) instead of 3-(2,4-difluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **60b**). Example **179** was obtained as a white solid (15 mg). LCMS ($M+H^+$): 402. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.53 (s, 1H), 8.14 (s, 1H), 7.74 - 7.70 (m, 2H), 7.62 - 7.56 (m, 1H), 7.39 - 7.35 (m, 1H), 7.19 (dt, *J*=2.2, 8.4 Hz, 1H), 5.17 (d, *J*=16.9 Hz, 1H), 4.98 - 4.94 (m, 1H), 4.51 (d, *J*=16.9 Hz, 1H), 4.31 - 4.24 (m, 1H), 4.20 - 4.15 (m, 1H), 2.26 (s, 3H), 1.18 (d, *J*=6.9 Hz, 3H).

Example 180:

N-cyclopentyl-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



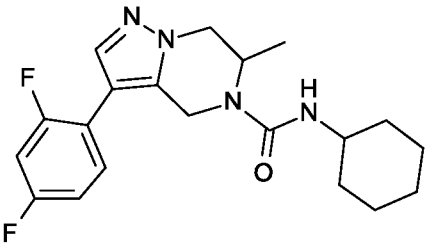
Preparation of Example 180:

The title compound was prepared in analogy to the preparation of Example **11** by using cyclopentanamine instead of 3-(trifluoromethyl)aniline and 3-(2,4-difluorophenyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **85b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **180** was obtained as a

white solid (9 mg). LCMS ($M+H^+$): 361. ^1H NMR (400MHz, DMSO-d_6) δ ppm 7.69 (d, *J*=2.1 Hz, 1H), 7.53 (dt, *J*=6.7, 8.8 Hz, 1H), 7.39 - 7.35 (m, 1H), 7.18 (dt, *J*=2.2, 8.4 Hz, 1H), 6.55 (d, *J*=6.9 Hz, 1H), 4.91 (d, *J*=16.9 Hz, 1H), 4.84 - 4.76 (m, 1H), 4.29 (d, *J*=16.8 Hz, 1H), 4.17 (dd, *J*=4.3, 12.7 Hz, 1H), 4.13 - 4.09 (m, 1H), 3.96 - 3.89 (m, 1H), 1.85 - 1.75 (m, 2H), 1.67 - 1.58 (m, 2H), 1.51 - 1.32 (m, 4H), 1.10 (d, *J*=6.8 Hz, 3H).

Example 181:

N-cyclohexyl-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

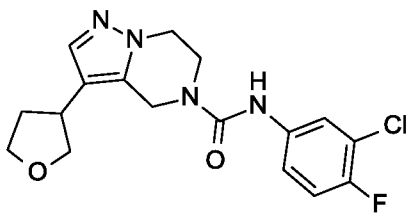


Preparation of Example 181:

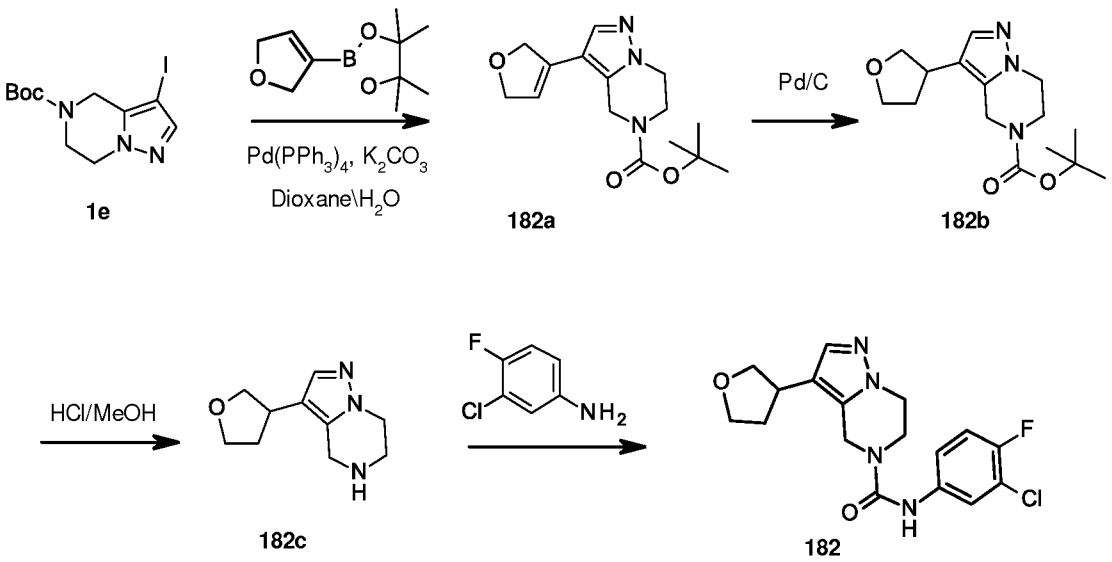
The title compound was prepared in analogy to the preparation of Example **11** by using cyclohexanamine instead of 3-(trifluoromethyl)aniline and 3-(2,4-difluorophenyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **85b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **181** was obtained as a white solid (2 mg). LCMS ($M+H^+$): 375. ^1H NMR (400MHz, DMSO-d_6) δ ppm 7.69 (d, *J*=2.3 Hz, 1H), 7.57 - 7.49 (m, 1H), 7.41 - 7.34 (m, 1H), 7.19 (t, *J*=8.2 Hz, 1H), 6.47 (d, *J*=8.2 Hz, 1H), 4.90 (d, *J*=17.1 Hz, 1H), 4.80 (s, 1H), 4.28 (d, *J*=17.2 Hz, 1H), 4.15 (d, *J*=4.8 Hz, 1H), 4.13 - 4.08 (m, 1H), 1.78 - 1.67 (m, 5H), 1.55 (br. s, 1H), 1.25 - 1.14 (m, 5H), 1.09 (d, J=6.8 Hz, 3H).

Example 182:

N-(3-chloro-4-fluoro-phenyl)-3-tetrahydrofuran-3-yl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of 3-tetrahydrofuran-3-yl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound 182c):

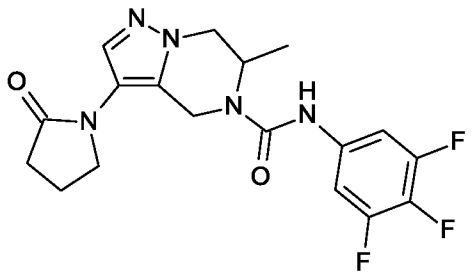
The compound **182c** was prepared in analogy to compound **26c** by using 2-(2,5-dihydrofuran-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane instead of cyclopenten-1-ylboronic acid. Compound **182c** was obtained as a white solid (60 mg). LCMS ($M+H^+$): 306.

Preparation of N-(3-chloro-4-fluoro-phenyl)-3-tetrahydrofuran-3-yl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 182):

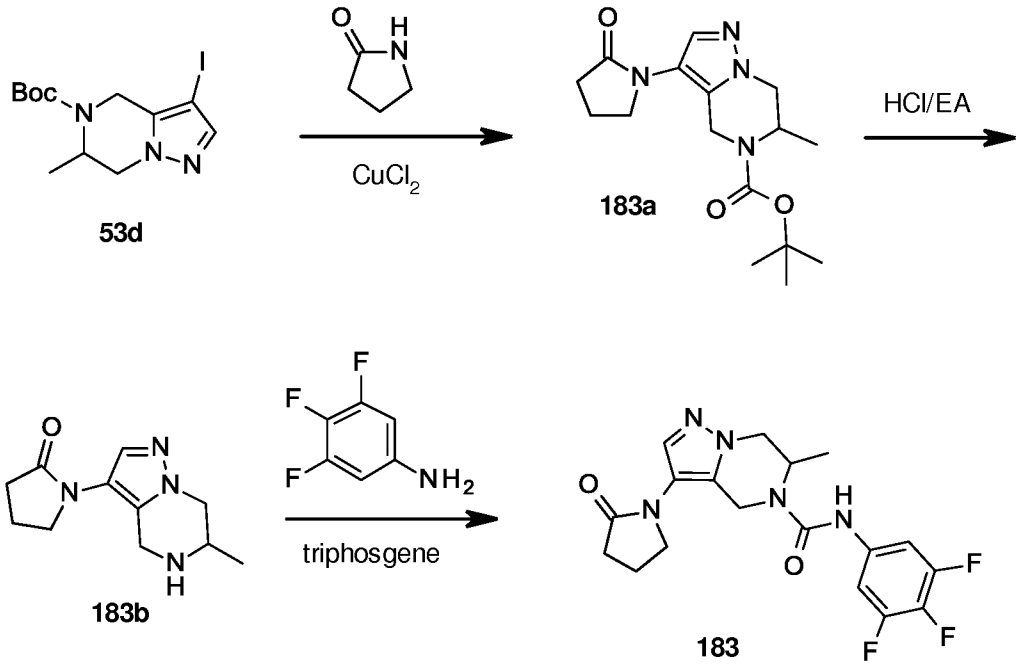
The title compound was prepared in analogy to the preparation of Example **11** by using 3-chloro-4-fluoroaniline instead of 3-(trifluoromethyl)aniline and 3-tetrahydrofuran-3-yl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **182c**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **182** was obtained as a white solid (13 mg). LCMS ($M+H^+$): 365. ^1H NMR (400MHz, CD_3OD) δ ppm 7.64 (dd, *J*=2.6, 6.7 Hz, 1H), 7.44 (s, 1H), 7.37 - 7.33 (m, 1H), 7.18 (t, *J*=9.0 Hz, 1H), 4.80 (d, *J*=2.0 Hz, 2H), 4.25 - 4.18 (m, 2H), 4.14 - 3.98 (m, 4H), 3.91 (q, *J*=7.6 Hz, 1H), 3.64 (t, *J*=7.8 Hz, 1H), 3.41 - 3.34 (m, 1H), 2.39 - 2.33 (m, 1H), 2.09 - 1.90 (m, 1H).

Example 183:

6-methyl-3-(2-oxopyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of 1-(6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)pyrrolidin-2-one (compound 183b):

The compound **183b** was prepared in analogy to the preparation of compound **170b** by using pyrollidin-2-one and tert-butyl 3-iodo-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **53d**) instead of tert-butyl 3-iodo-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **1e**). Compound **183** (240 mg) was obtained as a slight yellow solid. LCMS ($M+H^+$): 251.

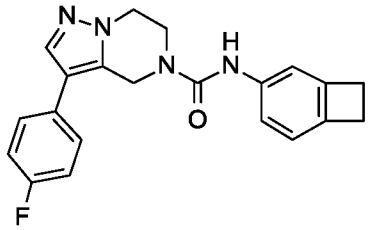
Preparation of 6-methyl-3-(2-oxopyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 183):

The title compound was prepared in analogy to the preparation of Example **170** by using 3,4,5-trifluoroaniline instead of 3-chloro-4-fluoro-aniline and 1-(6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)pyrrolidin-2-one (compound **183b**) instead of 1-(4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)pyrrolidin-2-one (compound **170b**). Example **183** was obtained as a white solid (23 mg). LCMS ($M+H^+$): 394. ^1H NMR (400MHz, DMSO-d_6) δ ppm

9.10 (s, 1H), 7.60 (s, 1H), 7.47 - 7.39 (m, 2H), 5.03 - 4.95 (m, 1H), 4.91 - 4.82 (m, 1H), 4.49 - 4.33 (m, 1H), 4.24 - 4.17 (m, 1H), 4.15 - 4.09 (m, 1H), 3.86 - 3.64 (m, 2H), 2.44 - 2.38 (m, 2H), 2.16 - 2.05 (m, 2H), 1.14 (d, *J*=6.8 Hz, 3H).

Example 184:

N-(4-bicyclo[4.2.0]octa-1(6),2,4-trienyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

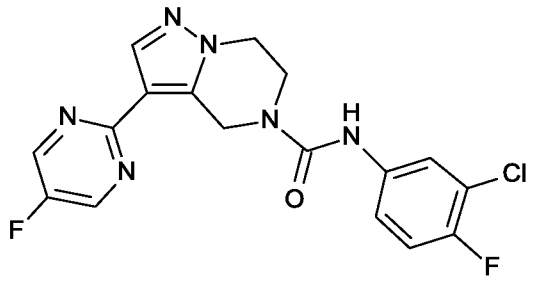


Preparation of Example 184:

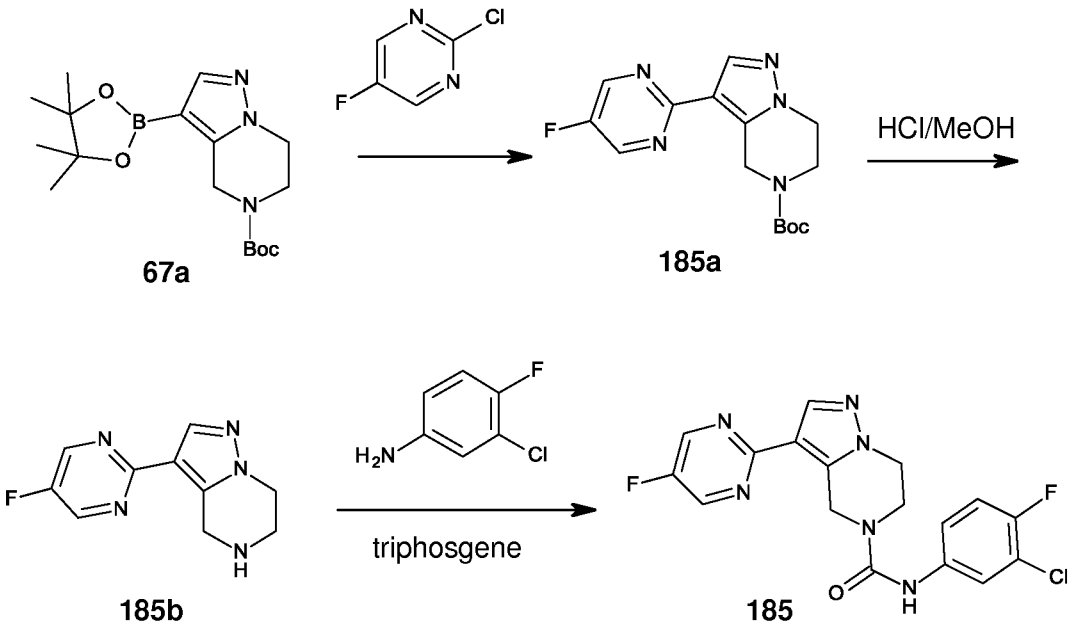
The title compound was prepared in analogy to the preparation of Example **11** by using bicyclo[4.2.0]octa-1,3,5-trien-4-amine (for its synthesis, refer to: US Patent 5,274,135) instead of 3-(trifluoromethyl)aniline Example **184** was obtained as a white solid (14 mg). LCMS ($M+H^+$): 363. ^1H NMR (400MHz, DMSO-d_6) δ ppm 8.78 (s, 1H), 7.83 (s, 1H), 7.49 (d, *J*=5.4 Hz, 2H), 7.27 (t, *J*=8.9 Hz, 2H), 7.22 - 7.19 (m, 1H), 7.17 - 7.12 (m, 1H), 6.96 (s, 1H), 4.91 (s, 2H), 4.22 - 4.18 (m, 2H), 3.99 (d, *J*=5.5 Hz, 2H), 3.06 (s, 4H).

Example 185:

N-(3-chloro-4-fluoro-phenyl)-3-(5-fluoropyrimidin-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



67a 185a

185b 185

Preparation of 3-(5-fluoropyrimidin-2-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound 185b):

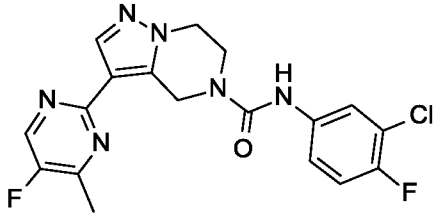
The compound **185b** was prepared in analogy to compound **67c** by using 2-chloro-5-fluoro-pyrimidine instead of 2-chloro-4-(trifluoromethyl)pyridine.

Preparation of N-(3-chloro-4-fluoro-phenyl)-3-(5-fluoropyrimidin-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 185):

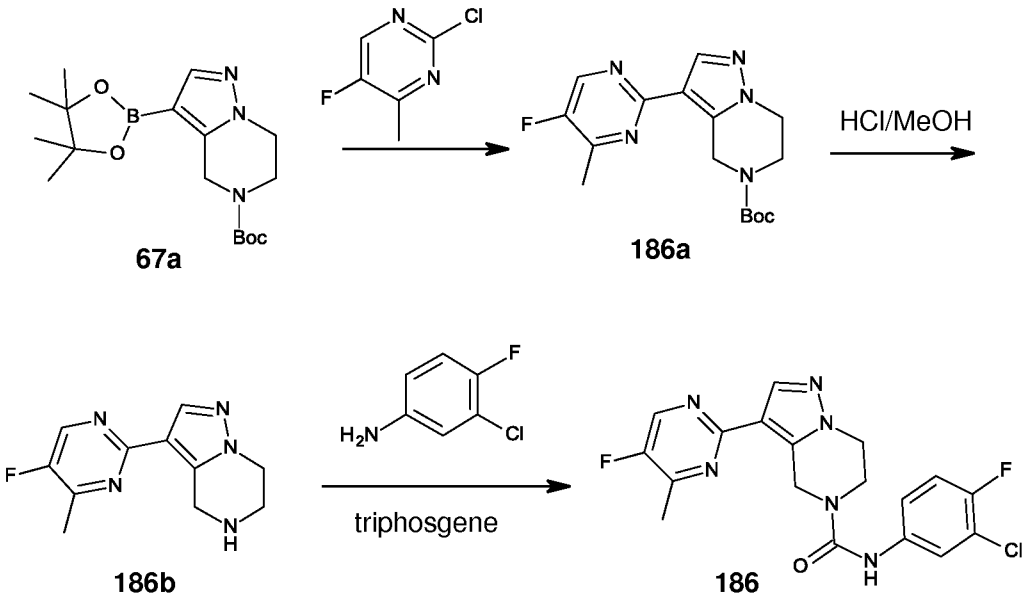
The title compound was prepared in analogy to the preparation of Example **170** by using 3-(5-fluoropyrimidin-2-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **185b**) instead of 1-(4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)pyrrolidin-2-one (compound **170b**). Example **185** was obtained as a white solid (28 mg). LCMS ($M+H^+$): 391. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.12 (s, 1H), 8.89 (s, 2H), 8.08 (s, 1H), 7.73 (dd, *J*=2.5, 6.9 Hz, 1H), 7.49 - 7.16 (m, 2H), 5.06 (s, 2H), 4.26 (br. s, 2H), 4.01 (d, *J*=5.5 Hz, 2H).

Example 186:

N-(3-chloro-4-fluoro-phenyl)-3-(5-fluoro-4-methyl-pyrimidin-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



67a 186a 186b 186

Preparation of 3-(5-fluoro-4-methyl-pyrimidin-2-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound 186b):

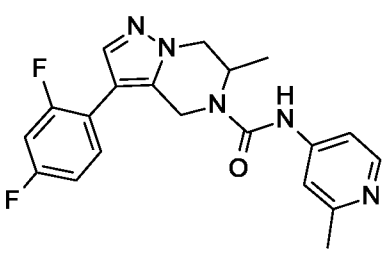
The compound **186b** was prepared in analogy to compound **67c** by using 2-chloro-5-fluoro-4-methyl-pyrimidine instead of 2-chloro-4-(trifluoromethyl)pyridine.

Preparation of N-(3-chloro-4-fluoro-phenyl)-3-(5-fluoro-4-methyl-pyrimidin-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 186):

The title compound was prepared in analogy to the preparation of Example **170** by using 3-(5-fluoro-4-methyl-pyrimidin-2-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **186b**) instead of 1-(4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)pyrrolidin-2-one (compound **170b**). Example **186** was obtained as a white solid (21 mg). LCMS ($M+H^+$): 405. ^1H NMR (400MHz, CD_3OD) δ ppm 8.51 (d, *J*=3.0 Hz, 1H), 8.13 (d, *J*=3.8 Hz, 1H), 7.61 (dd, *J*=2.6, 6.6 Hz, 1H), 7.40 - 7.27 (m, 1H), 7.16 (t, *J*=9.2 Hz, 1H), 5.17 (s, 2H), 4.30 (br, 2H), 4.13 - 4.01 (br, 2H), 2.55 (s, 3H).

Example 187:

3-(2,4-difluorophenyl)-6-methyl-N-(2-methyl-4-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

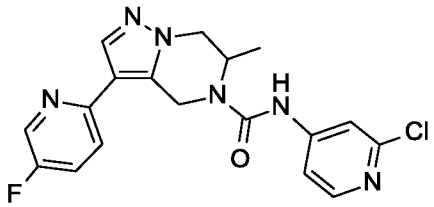


Preparation of Example 187:

The title compound was prepared in analogy to the preparation of Example **60** by using 2-methylpyridin-4-amine instead of 5-fluoro-6-methyl-pyridin-2-amine and 3-(2,4-difluorophenyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **85b**) instead of 3-(2,4-difluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **60b**). Example **187** was obtained as a white solid (32 mg). LCMS ($M+H^+$): 384. ^1H NMR (400MHz, CD_3OD) δ ppm 8.48 (d, *J*=6.3 Hz, 1H), 7.75 (br. s, 3H), 7.62 - 7.51 (m, 1H), 7.45 - 7.34 (m, 1H), 7.26 - 7.15 (m, 1H), 5.12 (d, *J*=17.1 Hz, 1H), 4.97 (br. s, 1H), 4.63 (d, *J*=16.8 Hz, 1H), 4.39 - 4.20 (m, 2H), 2.59 (s, 3H), 1.24 (d, J=6.4 Hz, 3H).

Example 188:

N-(2-chloro-4-pyridyl)-3-(5-fluoro-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

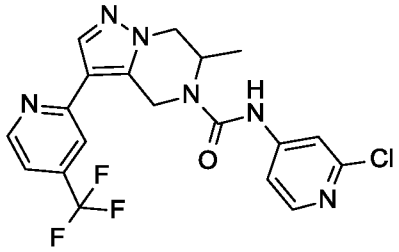


Preparation of Example 188:

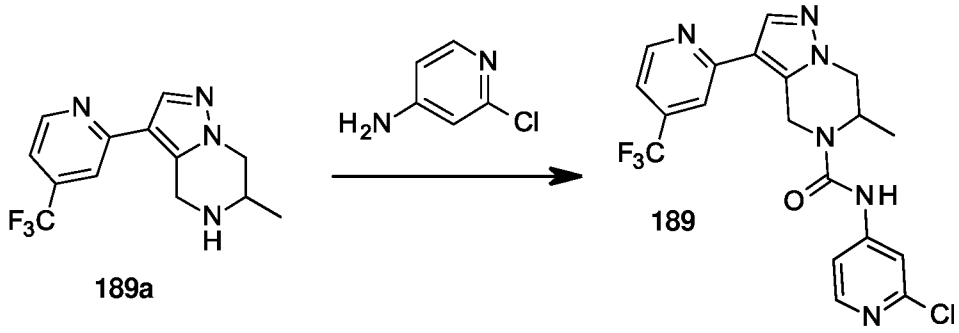
The title compound was prepared in analogy to the preparation of Example **60** by using 2-chloropyridin-4-amine instead of 5-fluoro-6-methyl-pyridin-2-amine and 3-(5-fluoro-2-pyridyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **94b**) instead of 3-(2,4-difluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **60b**). Example **188** was obtained as a white solid (26 mg). LCMS ($M+H^+$): 387. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.79 (s, 1H), 8.60 - 8.58 (m, 1H), 8.21 - 8.18 (m, 1H), 8.15 (s, 1H), 7.88 - 7.75 (m, 2H), 7.72 - 7.70 (m, 1H), 7.59 - 7.48 (m, 1H), 5.51 - 5.44 (m, 1H), 5.03 - 4.94 (m, 1H), 4.71 - 4.61 (m, 1H), 4.36 - 4.30 (m, 1H), 4.22 - 4.17 (m, 1H), 1.19 (d, *J*=6.8 Hz, 3H).

Example 189:

N-(2-chloro-4-pyridyl)-6-methyl-3-[4-(trifluoromethyl)-2-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



Preparation of Example 189:



189a

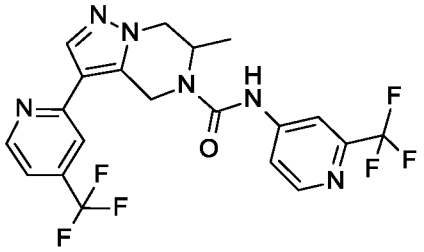
189

The compound **189a** was prepared in analogy to compound **67c** by using tert-butyl 3-iodo-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **53d**) instead of tert-butyl 3-iodo-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **1e**).

The Example **189** was prepared in analogy to the preparation of Example **60** by using 2-chloropyridin-4-amine instead of 5-fluoro-6-methyl-pyridin-2-amine and 6-methyl-3-[4-(trifluoromethyl)-2-pyridyl]-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **189a**) instead of 3-(2,4-difluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **60b**). Example **189** was obtained as a white solid (10 mg). LCMS ($M+H^+$): 437. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.73(s, 1H), 8.87 - 8.84 (m, 1H), 8.39 (s, 1H), 8.20 - 8.17 (m, 1H), 8.12 - 8.10 (m, 1H), 7.69 (s, 1H), 7.54 - 7.50 (m, 2H), 5.52 (d, *J*=18.4 Hz, 1H), 5.01 - 4.91 (m, 1H), 4.71 - 4.65 (m, 1H), 4.38 - 4.31 (m, 1H), 4.23 (br, 1H), 1.20 (d, *J*=6.8 Hz, 3H).

Example 190:

6-methyl-N-[2-(trifluoromethyl)-4-pyridyl]-3-[4-(trifluoromethyl)-2-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

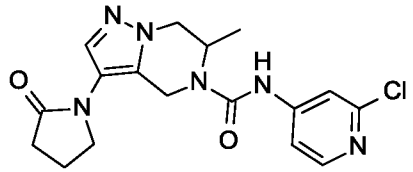


Preparation of Example 190:

The title compound was prepared in analogy to the preparation of Example **60** by using 2-trifluoromethylpyridin-4-amine instead of 5-fluoro-6-methyl-pyridin-2-amine and 36-methyl-3-[4-(trifluoromethyl)-2-pyridyl]-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **189a**) instead of 3-(2,4-difluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **60b**). Example **190** was obtained as a white solid (13 mg). LCMS ($M+H^+$): 471. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.76(s, 1H), 8.88 - 8.85 (m, 1H), 8.54 - 8.52 (m, 1H), 8.40 (s, 1H), 8.13 - 8.11 (m, 1H), 8.07 - 8.05 (m, 1H), 7.78 - 7.74 (m, 1H), 7.55 - 7.51 (m, 1H), 5.57 - 5.48 (m, 1H), 4.99 - 4.93 (m, 1H), 4.74 - 4.66 (m, 1H), 4.39 - 4.32 (m, 1H), 4.27 - 4.19 (m, 1H), 1.21 (d, *J*=6.8 Hz, 3H).

Example 191:

N-(2-chloro-4-pyridyl)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

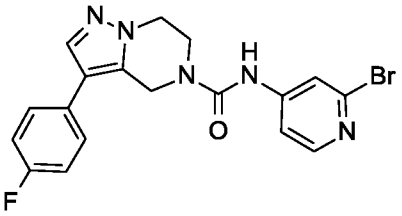


Preparation of Example 191:

The title compound was prepared in analogy to the preparation of Example **60** by using 2-chloropyridin-4-amine instead of 5-fluoro-6-methyl-pyridin-2-amine and 1-(6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)pyrrolidin-2-one (compound **183b**) instead of 3-(2,4-difluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **60b**). Example **191** was obtained as a white solid (27 mg). LCMS ($M+H^+$): 375. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.56 (s, 1H), 8.16 (d, *J*=5.7 Hz, 1H), 7.67 (d, *J*=1.5 Hz, 1H), 7.60 (s, 1H), 7.53 - 7.43 (m, 1H), 5.11 - 5.00 (m, 1H), 4.95 - 4.83 (m, 1H), 4.47 - 4.36 (m, 1H), 4.27 - 4.18 (m, 1H), 4.15 - 4.07 (m, 1H), 3.85 - 3.63 (m, 2H), 2.40 (s, 2H), 2.10 (d, *J*=7.7 Hz, 2H), 1.14 (d, J=6.6 Hz, 3H).

Example 192:

N-(2-bromo-4-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

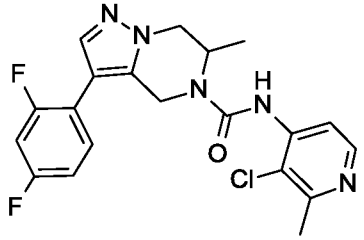


Preparation of Example 192:

The title compound was prepared in analogy to the preparation of Example **60** by using 2-bromopyridin-4-amine instead of 5-fluoro-6-methyl-pyridin-2-amine and 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**) instead of 3-(2,4-difluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **60b**). Example **192** was obtained as a white solid (7 mg). LCMS ($M+H^+$): 416. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.49 (s, 1H), 8.15 (d, *J*=5.6 Hz, 1H), 7.84 (s, 1H), 7.77 (d, *J*=1.9 Hz, 1H), 7.53 - 7.46 (m, 3H), 7.28 (t, *J*=8.9 Hz, 2H), 4.95 (s, 2H), 4.23 (d, *J*=5.3 Hz, 2H), 4.07 - 3.98 (m, 2H).

Example 193:

N-(3-chloro-2-methyl-4-pyridyl)-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

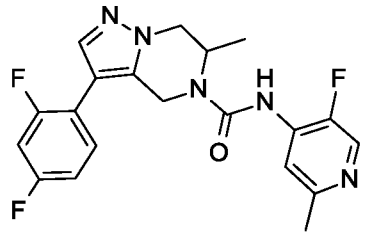


Preparation of Example 193:

The title compound was prepared in analogy to the preparation of Example **60** by using 3-chloro-2-methyl-pyridin-4-amine instead of 5-fluoro-6-methyl-pyridin-2-amine and 3-(2,4-difluorophenyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **85b**) instead of 3-(2,4-difluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **60b**). Example **193** was obtained as a white solid (12 mg). LCMS ($M+H^+$): 418. ^1H NMR (400MHz, DMSO-d_6) δ ppm 8.62 (s, 1H), 8.23 (d, *J*=5.5 Hz, 1H), 7.74 (d, *J*=1.9 Hz, 1H), 7.59 - 7.52 (m, 2H), 7.43 - 7.34 (m, 1H), 7.23 - 7.15 (m, 1H), 5.08 (d, *J*=16.4 Hz, 1H), 4.90 (d, *J*=5.4 Hz, 1H), 4.60 (d, *J*=16.8 Hz, 1H), 4.33 (dd, *J*=4.4, 12.5 Hz, 1H), 4.25 - 4.19 (m, 1H), 1.20 (d, *J*=6.9 Hz, 3H).

Example 194:

3-(2,4-difluorophenyl)-N-(5-fluoro-2-methyl-4-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

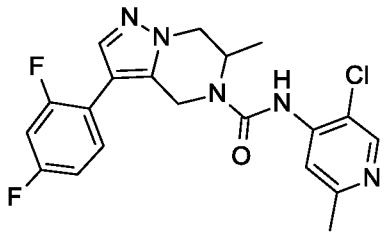


Preparation of Example 194:

The title compound was prepared in analogy to the preparation of Example **60** by using 5-fluoro-2-methyl-pyridin-4-amine instead of 5-fluoro-6-methyl-pyridin-2-amine and 3-(2,4-difluorophenyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **85b**) instead of 3-(2,4-difluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **60b**). Example **194** was obtained as a white solid (40 mg). LCMS ($M+H^+$): 402. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.00 (br. s, 1H), 8.30 (d, *J*=2.9 Hz, 1H), 7.74 (d, *J*=2.0 Hz, 1H), 7.56 (dt, *J*=6.6, 8.8 Hz, 1H), 7.50 (d, *J*=6.5 Hz, 1H), 7.42 - 7.33 (m, 1H), 7.23 - 7.15 (m, 1H), 5.08 (d, *J*=17.1 Hz, 1H), 4.96 - 4.85 (m, 1H), 4.56 (d, *J*=16.9 Hz, 1H), 4.35 - 4.26 (m, 1H), 4.24 - 4.15 (m, 1H), 2.38 (s, 3H), 1.20 (d, *J*=6.8 Hz, 3H).

Example 195:

N-(5-chloro-2-methyl-4-pyridyl)-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



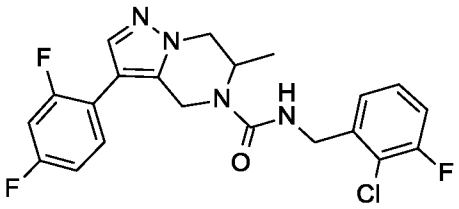
Preparation of Example 195:

The title compound was prepared in analogy to the preparation of Example **60** by using 5-chloro-2-methyl-pyridin-4-amine instead of 5-fluoro-6-methyl-pyridin-2-amine and 3-(2,4-difluorophenyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **85b**) instead of 3-(2,4-difluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **60b**). Example **195**

was obtained as a white solid (10 mg). LCMS ($M+H^+$): 418. ^1H NMR (400MHz, DMSO-d_6) δ ppm 8.68 (br. s, 1H), 8.38 (s, 1H), 7.74 (d, *J*=1.9 Hz, 1H), 7.59 - 7.54 (m, 1H), 7.53 (s, 1H), 7.44 - 7.34 (m, 1H), 7.19 (dt, *J*=2.3, 8.4 Hz, 1H), 5.08 (d, *J*=16.7 Hz, 1H), 4.95 - 4.85 (m, 1H), 4.59 (d, *J*=16.8 Hz, 1H), 4.37 - 4.28 (m, 1H), 4.25 - 4.18 (m, 1H), 2.41 (s, 3H), 1.20 (d, *J*=6.8 Hz, 3H).

Example 196:

N-[(2-chloro-3-fluoro-phenyl)methyl]-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

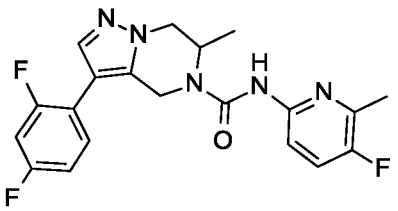


Preparation of Example 196:

The title compound was prepared in analogy to the preparation of Example **11** by using (2-chloro-3-fluoro-phenyl)methanamine instead of 3-(trifluoromethyl)aniline and 3-(2,4-difluorophenyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **85b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **196** was obtained as a white solid (11 mg). LCMS ($M+H^+$): 435. ^1H NMR (400MHz, DMSO-d_6) δ ppm 7.72 (d, *J*=2.1 Hz, 1H), 7.55 (dt, *J*=6.6, 8.8 Hz, 1H), 7.47 (t, *J*=5.3 Hz, 1H), 7.41 - 7.26 (m, 3H), 7.21 - 7.14 (m, 2H), 4.97 (d, *J*=16.8 Hz, 1H), 4.87 - 4.79 (m, 1H), 4.45 - 4.35 (m, 3H), 4.27 - 4.21 (m, 1H), 4.19 - 4.14 (m, 1H), 1.13 (d, *J*=6.8 Hz, 3H).

Example 197:

3-(2,4-difluorophenyl)-N-(5-fluoro-6-methyl-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



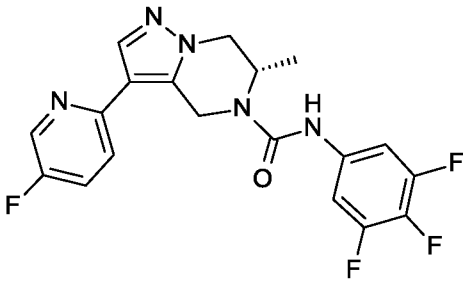
Preparation of Example 197:

The title compound was prepared in analogy to the preparation of Example **60** by using 3-fluoro-2-methyl-pyridin-4-amine instead of 5-fluoro-6-methyl-pyridin-2-amine and 3-(2,4-difluorophenyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **85b**) instead of

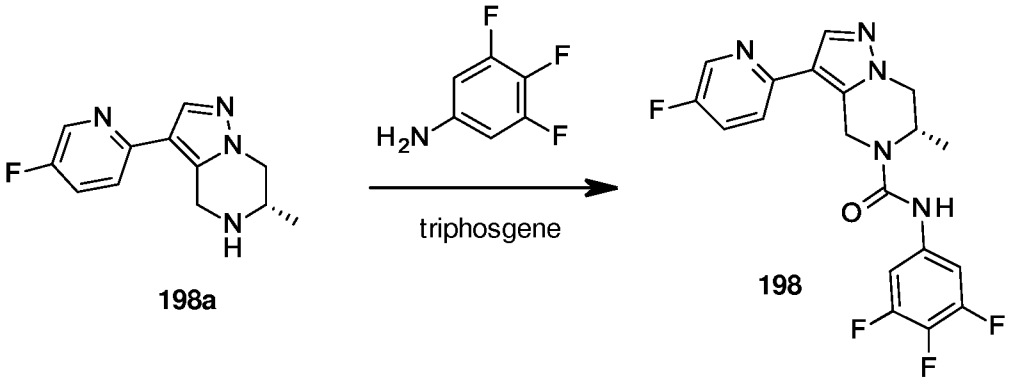
3-(2,4-difluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **60b**). Example **197** was obtained as a white solid (6 mg). LCMS ($M+H^+$): 402. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.53 (s, 1H), 7.72 (d, *J*=2.1 Hz, 1H), 7.67 - 7.62 (m, 1H), 7.60 - 7.54 (m, 2H), 7.42 - 7.33 (m, 1H), 7.20 (dt, *J*=2.1, 8.5 Hz, 1H), 5.16 (d, *J*=16.8 Hz, 1H), 5.00 - 4.92 (m, 1H), 4.51 (d, *J*=17.1 Hz, 1H), 4.32 - 4.24 (m, 1H), 4.20 - 4.13 (m, 1H), 2.37 (d, *J*=2.9 Hz, 3H), 1.17 (d, *J*=6.9 Hz, 3H).

Example 198:

(6S)-3-(5-fluoro-2-pyridyl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



Preparation of Example 198:



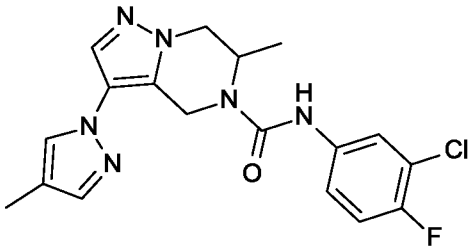
The compound **198a** was prepared in analogy to compound **67c** by using 2-chloro-5-fluoro-pyridine instead of 2-chloro-4-(trifluoromethyl)pyridine and (6S)-tert-butyl 3-iodo-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **102d**) instead of tert-butyl 3-iodo-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **1e**).

The Example **198** was prepared in analogy to the preparation of Example **11** by using 3,4,5-trifluoroaniline instead of 3-(trifluoromethyl)aniline and (6S)-3-(5-fluoro-2-pyridyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **198a**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **198** was obtained as a white solid (6 mg). LCMS ($M+H^+$): 406. ^1H NMR (400MHz, DMSO-d_6) δ ppm

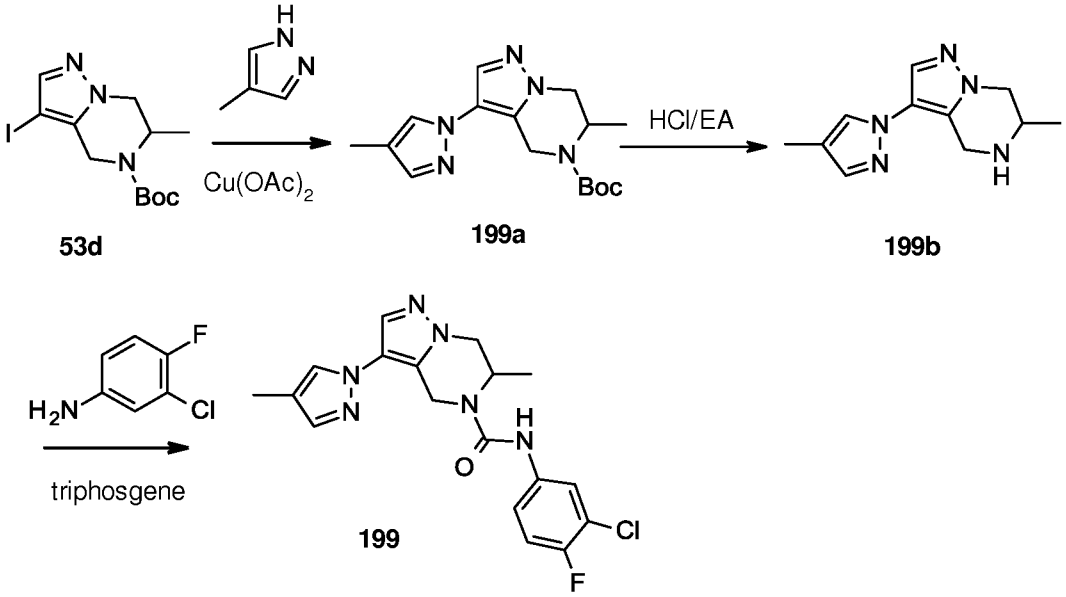
9.21 (s, 1H), 8.59 - 8.57 (m, 1H), 8.14 (s, 1H), 7.85 - 7.71 (m, 2H), 7.51 - 7.37 (m, 2H), 5.46 - 5.38 (m, 1H), 4.93 - 4.82 (m, 1H), 4.68 - 4.57 (m, 1H), 4.33 - 4.26 (m, 1H), 4.24 - 4.16 (m, 1H), 1.20 - 1.14 (m, 3H).

Example 199:

N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(4-methylpyrazol-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



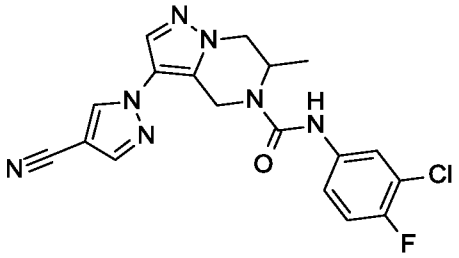
Preparation of N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(4-methylpyrazol-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 199)

The title compound was prepared in analogy to the preparation of Example **171** by using tert-butyl 3-iodo-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **53d**) instead of tert-butyl 3-iodo-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **1e**). Example **199** was obtained as a white solid (10 mg). LCMS ($M+H^+$): 389. ^1H NMR (400MHz, CD_3OD) δ ppm 7.78 (d, *J*=13.3 Hz, 2H), 7.62 (dd, *J*=2.6, 6.7 Hz, 1H), 7.53 (s, 1H), 7.36 - 7.29 (m, 1H), 7.16 (t, *J*=9.0 Hz, 1H), 5.22 (d, *J*=17.1 Hz, 1H), 5.08 - 4.96 (m, 1H),

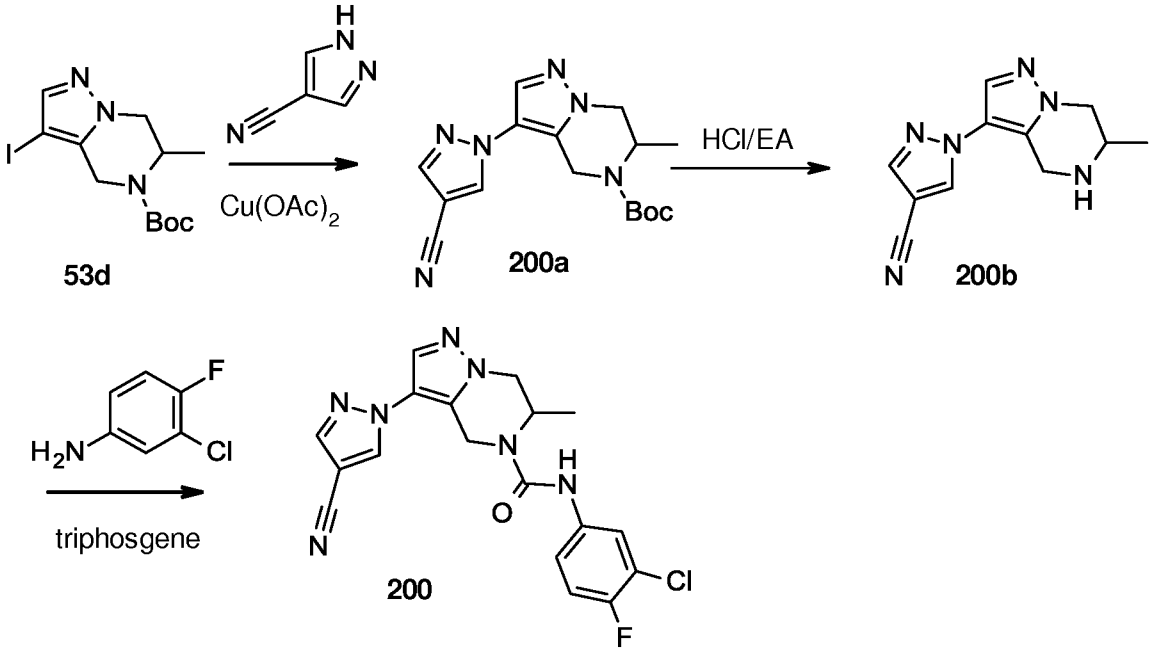
4.67 (d, *J*=17.1 Hz, 1H), 4.40 - 4.30 (m, 1H), 4.26 - 4.12 (m, 1H), 2.17 (s, 3H), 1.29 (d, *J*=6.9 Hz, 3H).

Example 200:

N-(3-chloro-4-fluoro-phenyl)-3-(4-cyanopyrazol-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



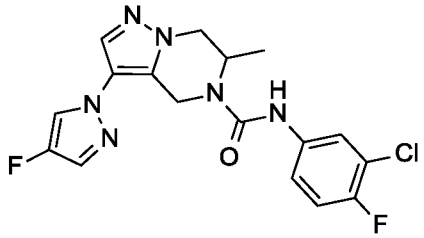
Preparation of N-(3-chloro-4-fluoro-phenyl)-3-(4-cyanopyrazol-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 200):

The title compound was prepared in analogy to the preparation of Example **171** by using tert-butyl 3-iodo-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **53d**) instead of tert-butyl 3-iodo-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **1e**) and 1H-pyrazole-4-carbonitrile instead of 4-methyl-1H-pyrazole. Example **200** was obtained as a white solid (5 mg). LCMS ($M+H^+$): 400. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.06 - 8.98 (m, 2H), 8.36 (s, 1H), 7.99 (s, 1H), 7.73 (dd, *J*=2.5, 6.9 Hz, 1H), 7.45 - 7.38 (m,

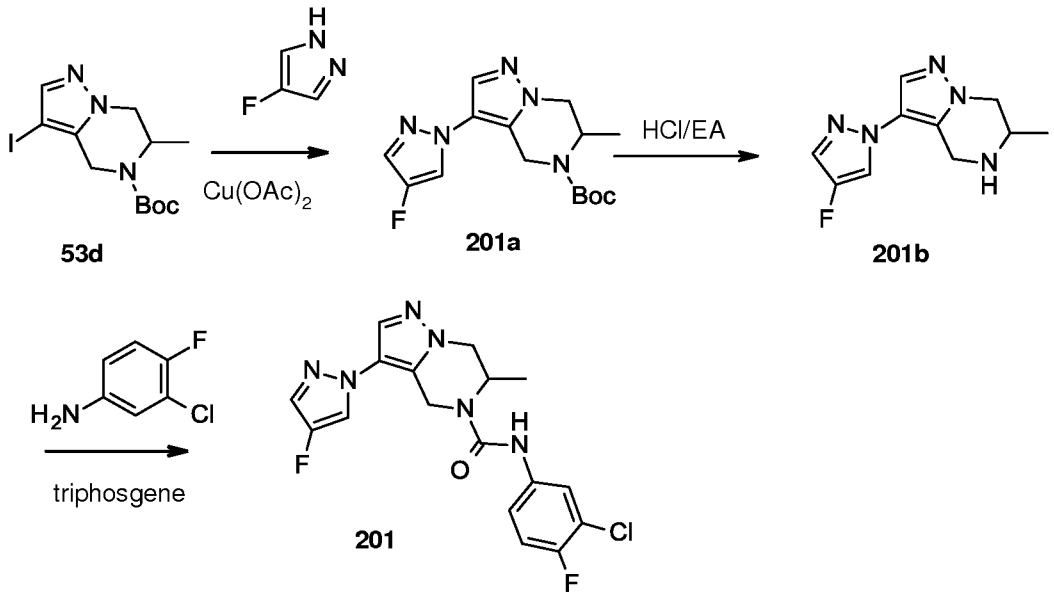
1H), 7.36 - 7.29 (m, 1H), 5.26 (d, *J*=17.4 Hz, 1H), 4.95 - 4.87 (m, 1H), 4.55 (d, *J*=17.4 Hz, 1H), 4.33 - 4.25 (m, 1H), 4.23 - 4.16 (m, 1H), 1.18 (d, *J*=6.9 Hz, 3H).

Example 201:

N-(3-chloro-4-fluoro-phenyl)-3-(4-fluoropyrazol-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:

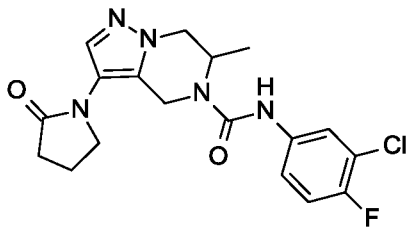


Preparation of N-(3-chloro-4-fluoro-phenyl)-3-(4-fluoropyrazol-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 201):

The title compound was prepared in analogy to the preparation of Example **171** by using tert-butyl 3-iodo-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **53d**) instead of tert-butyl 3-iodo-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **1e**) and 4-fluoro-1H-pyrazole instead of 4-methyl-1H-pyrazole. Example **201** was obtained as a white solid (15 mg). LCMS ($M+H^+$): 393. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.00 (s, 1H), 8.40 (d, *J*=4.3 Hz, 1H), 7.88 (s, 1H), 7.82 - 7.71 (m, 2H), 7.45 - 7.39 (m, 1H), 7.33 (t, *J*=9.1 Hz, 1H), 5.24 (d, *J*=17.6 Hz, 1H), 4.90 (d, *J*=3.8 Hz, 1H), 4.53 (d, *J*=17.6 Hz, 1H), 4.31 - 4.23 (m, 1H), 4.21 - 4.14 (m, 1H), 1.17 (d, *J*=6.8 Hz, 3H).

Example 202:

N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

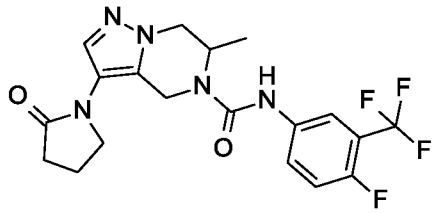


Preparation of Example 202:

The title compound was prepared in analogy to the preparation of Example **170** by using 1-(6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)pyrrolidin-2-one (compound **183b**) instead of 1-(4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)pyrrolidin-2-one (compound **170b**). Example **202** was obtained as a white solid (15 mg). LCMS ($M+H^+$): 392. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.05 (s, 1H), 7.75 (s, 1H), 7.61 (s, 1H), 7.49 - 7.43 (m, 1H), 7.32 (s, 1H), 5.07 - 4.97 (m, 1H), 4.94 - 4.84 (m, 1H), 4.42 - 4.34 (m, 1H), 4.22 - 4.18 (m, 2H), 3.85 - 3.68 (m, 2H), 2.44 - 2.37 (m, 2H), 2.15 - 2.05 (m, 2H), 1.13 (d, J=6.8 Hz, 3H).

Example 203:

N-[4-fluoro-3-(trifluoromethyl)phenyl]-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



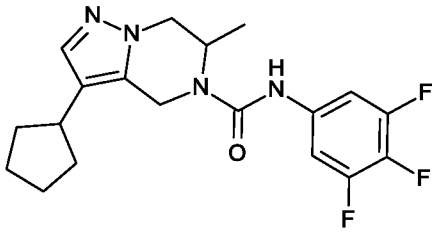
Preparation of Example 203:

The title compound was prepared in analogy to the preparation of Example **170** by using 4-fluoro-3-(trifluoromethyl)aniline instead of 3-chloro-4-fluoro-aniline and 1-(6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)pyrrolidin-2-one one (compound **183b**) instead of 1-(4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)pyrrolidin-2-one (compound **170b**). Example **203** was obtained as a white solid (13 mg). LCMS ($M+H^+$): 426. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.15 (s, 1H), 7.96 - 7.92 (m, 1H), 7.84 - 7.78 (m, 1H), 7.61 (s, 1H), 7.48 - 7.38 (m, 1H),

5.11 - 4.97 (m, 1H), 4.94 - 4.84 (m, 1H), 4.47 - 4.34 (m, 1H), 4.25 - 4.17 (m, 1H), 4.15 - 4.08 (m, 1H), 3.84 - 3.77 (m, 2H), 2.44 - 2.37 (m, 2H), 2.15 - 2.02 (m, 2H), 1.14 (d, *J*=6.8 Hz, 3H).

Example 204:

3-cyclopentyl-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

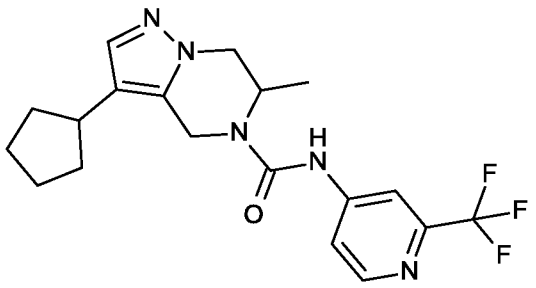


Preparation of Example 204:

The title compound was prepared in analogy to the preparation of Example **106** by using 3,4,5-trifluoroaniline instead of 3-amino-5-fluoro-benzonitrile and 3-cyclopentyl-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **96c**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **204** was obtained as a white solid (12 mg). LCMS ($M+H^+$): 379. ^1H NMR (400MHz, CD_3OD) δ ppm 7.43 - 7.37 (m, 1H), 7.35 - 7.27 (m, 2H), 5.03 (d, *J*=16.3 Hz, 1H), 4.97 - 4.91 (m, 1H), 4.49 (d, *J*=16.3 Hz, 1H), 4.26 (dd, *J*=4.3, 12.5 Hz, 1H), 4.16 - 4.10 (m, 1H), 2.99 - 2.93 (m, 1H), 2.18 - 1.98 (m, 2H), 1.89 - 1.78 (m, 2H), 1.77 - 1.65 (m, 2H), 1.63 - 1.50 (m, 2H), 1.21 (d, *J*=6.8 Hz, 3H).

Example 205:

3-cyclopentyl-6-methyl-N-[2-(trifluoromethyl)-4-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



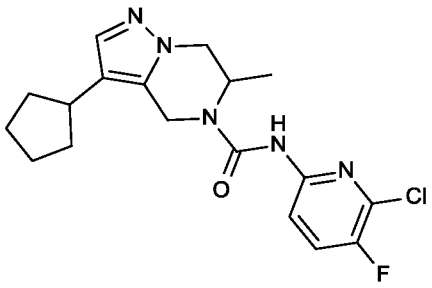
Preparation of Example 205:

The title compound was prepared in analogy to the preparation of Example **106** by using 2-(trifluoromethyl)pyridin-4-amine instead of 3-amino-5-fluoro-benzonitrile and 3-cyclopentyl-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **96c**) instead of 3-(4-

fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **205** was obtained as a white solid (2 mg). LCMS ($M+H^+$): 394. ^1H NMR (400MHz, CD_3OD) δ ppm 8.50 (d, *J*=5.5 Hz, 1H), 8.06 (d, *J*=2.0 Hz, 1H), 7.78 (dd, *J*=2.1, 5.6 Hz, 1H), 7.41 (s, 1H), 5.10 (d, *J*=16.3 Hz, 1H), 5.03 - 4.94 (m, 1H), 4.55 (d, *J*=16.3 Hz, 1H), 4.29 (dd, *J*=4.1, 12.7 Hz, 1H), 4.15 (dd, *J*=1.1, 12.7 Hz, 1H), 3.05 - 2.86 (m, 1H), 2.15 - 2.03 (m, 2H), 1.90 - 1.79 (m, 2H), 1.78 - 1.68 (m, 2H), 1.64 - 1.52 (m, 2H), 1.24 (d, *J*=6.8 Hz, 3H).

Example 206:

N-(6-chloro-5-fluoro-2-pyridyl)-3-cyclopentyl-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

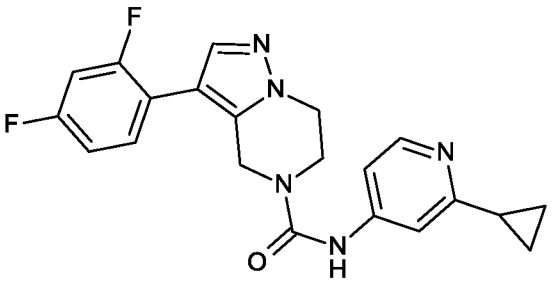


Preparation of Example 206:

The title compound was prepared in analogy to the preparation of Example **140** by using 3-cyclopentyl-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **96c**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **206** was obtained as a white solid (6 mg). LCMS ($M+H^+$): 378. ^1H NMR (400MHz, CD_3OD) δ ppm 7.85 (dd, *J*=3.1, 8.9 Hz, 1H), 7.67 (dd, *J*=7.9, 8.9 Hz, 1H), 7.39 (s, 1H), 5.06 (d, *J*=16.6 Hz, 1H), 4.99-4.93 (m, 1H), 4.51 (d, *J*=16.3 Hz, 1H), 4.27 (dd, *J*=4.4, 12.7 Hz, 1H), 4.12 (dd, *J*=1.3, 12.8 Hz, 1H), 3.02 - 2.84 (m, 1H), 2.14 - 2.02 (m, 2H), 1.89 - 1.64 (m, 4H), 1.63 - 1.50 (m, 2H), 1.23 (d, *J*=6.8 Hz, 3H).

Example 207:

N-(2-cyclopropyl-4-pyridyl)-3-(2,4-difluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

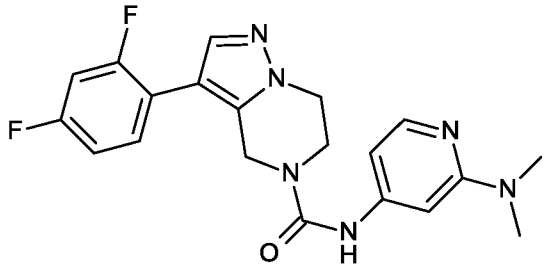


Preparation of Example 207:

The title compound was prepared in analogy to the preparation of Example **106** by using 2-cyclopropylpyridin-4-amine (AB140912, Shanghai AQBioPharma Co. Ltd) instead of 3-amino-5-fluoro-benzonitrile and 3-(2,4-difluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **50b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **207** was obtained as a white solid (7 mg). LCMS ($M+H^+$): 396. ^1H NMR (400MHz, CD_3OD) δ ppm 8.28 (d, *J*=7.0 Hz, 1H), 7.78 (dd, *J*=2.3, 7.0 Hz, 1H), 7.72 (d, *J*=1.3 Hz, 1H), 7.58 (d, *J*=2.0 Hz, 1H), 7.53 - 7.43 (m, 1H), 7.17 - 7.04 (m, 2H), 4.92 (s, 2H), 4.35 (t, *J*=5.5 Hz, 2H), 4.16 (t, *J*=5.5 Hz, 2H), 2.26 - 2.19 (m, 1H), 1.46 - 1.33 (m, 2H), 1.16 - 1.05 (m, 2H).

Example 208:

3-(2,4-difluorophenyl)-N-[2-(dimethylamino)-4-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



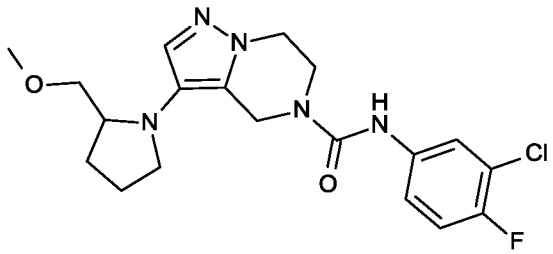
Preparation of Example 208:

The title compound was prepared in analogy to the preparation of Example **106** by using N2,N2-dimethylpyridine-2,4-diamine (catalog number: AQ14094, Shanghai AQBioPharma Co. Ltd) instead of 3-amino-5-fluoro-benzonitrile and 3-(2,4-difluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **50b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **208** was obtained as a white solid (26 mg). LCMS ($M+H^+$): 399. ^1H NMR (400MHz, CD_3OD) δ ppm 7.79 (d, *J*=6.8 Hz, 1H), 7.72

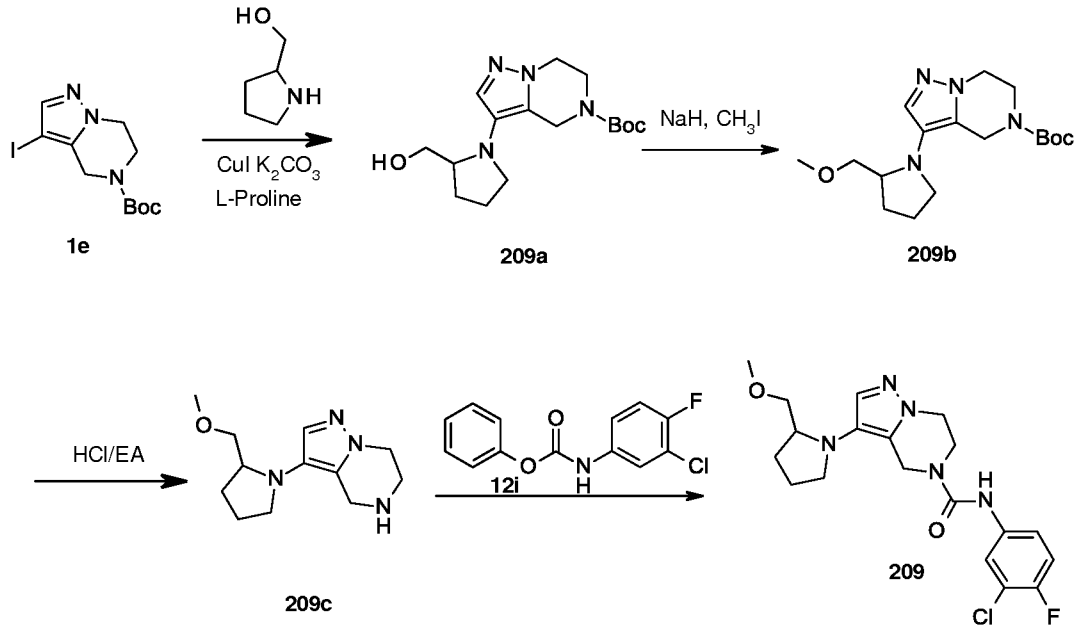
(d, *J*=1.5 Hz, 1H), 7.54 - 7.42 (m, 1H), 7.17 - 7.02 (m, 3H), 6.89 (dd, *J*=1.9, 6.7 Hz, 1H), 4.89 (s, 2H), 4.33 (t, *J*=5.5 Hz, 2H), 4.13 (t, *J*=5.5 Hz, 2H), 3.14 (s, 6H).

Example 209:

N-(3-chloro-4-fluoro-phenyl)-3-[2-(methoxymethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: **preparation of [1-(5-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl)pyrrolidin-2-yl]methanol (compound 209a)**

A mixture of tert-butyl 3-iodo-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **1e**, 175 mg 0.5 mmol), pyrrolidin-2-ylmethanol (100 mg, 1.0 mmol), L-proline (23 mg, 0.2 mmol), CuI (19 mg 0.1 mmol) and K_2CO_3 (207 mg, 1.5 mmol) in DMSO (5 mL) was stirred in microwave for 2 hours at 120 °C. The reaction mixture was diluted with water, extracted with EtOAc. The organic layer was concentrated. The residue was purified by column chromatography to afford compound **209a** (150 mg) as a slight yellow oil. LCMS ($M+H^+$): 323.

Step 2: preparation of tert-butyl 3-[2-(methoxymethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 209b)

To a solution of [1-(5-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl)pyrrolidin-2-yl]methanol (compound **209a**, 67 mg, 0.3 mmol) in THF (10 mL) was added NaH (36 mg, 0.6 mmol, 60% oil dispersion) slowly at room temperature and then Methyl iodide (85 mg, 0.6 mmol). The reaction mixture was stirred at room temperature for 2 hours and then was quenched with water, extracted with EtOAc. The organic layer was dried and concentrated in *vacuo* to afford compound **209b** (70 mg) as a slight yellow oil. LCMS ($M+H^+$): 337.

Step 3: preparation of 3-[2-(methoxymethyl)pyrrolidin-1-yl]-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound 209c)

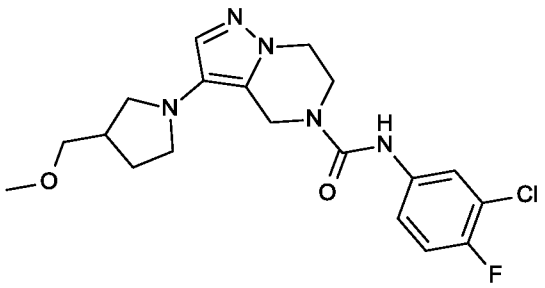
A solution of tert-butyl 3-[2-(methoxymethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **209b**, 70 mg, 0.3 mmol) in HCl/EA (10 mL) was stirred at room temperature for 2 hours. Then the reaction mixture was concentrated in *vacuo* to afford compound **209c** (60 mg) as a slight yellow solid. LCMS ($M+H^+$): 237.

Step 4: preparation of N-(3-chloro-4-fluoro-phenyl)-3-[2-(methoxymethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 209)

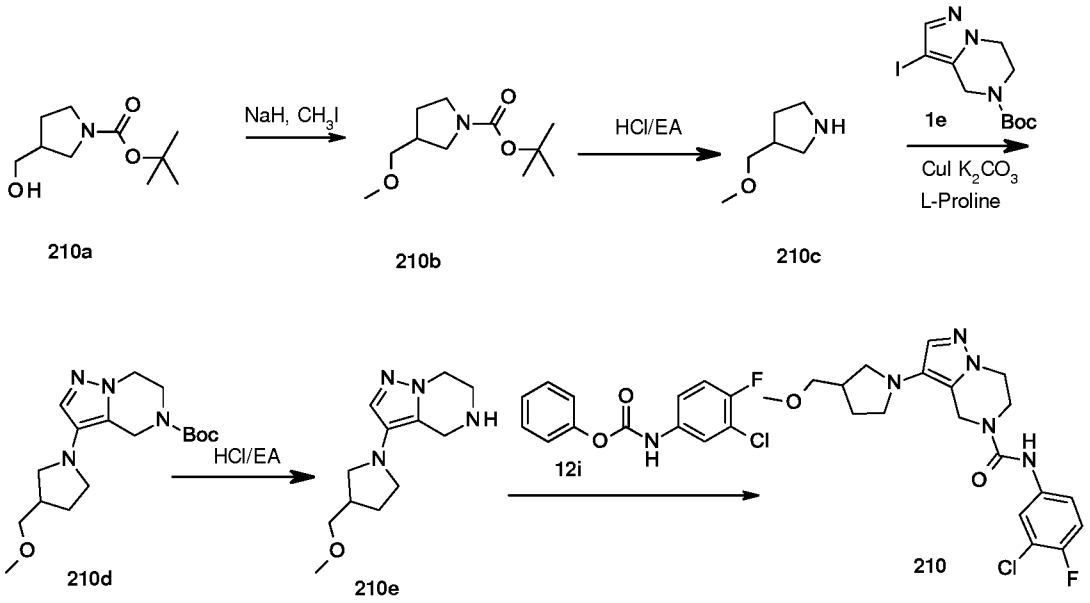
The title compound was prepared in analogy to the preparation of Example **140** by using phenyl N-(3-chloro-4-fluoro-phenyl)carbamate (compound **12i**) instead of phenyl N-(6-chloro-5-fluoro-2-pyridyl)carbamate (compound **140d**) and 3-[2-(methoxymethyl)pyrrolidin-1-yl]-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **209c**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **209** was obtained as a white solid (5 mg). LCMS ($M+H^+$): 408. ^1H NMR (400MHz, CD_3OD) δ ppm 7.63 (dd, *J*=2.6, 6.7 Hz, 1H), 7.38 - 7.29 (m, 2H), 7.17 (t, *J*=8.9 Hz, 1H), 4.84 (d, *J*=16.3 Hz, 1H), 4.76 (d, *J*=16.3 Hz, 1H), 4.62 (br. s, 2H), 4.23 - 4.14 (m, 2H), 4.13 - 4.03 (m, 1H), 3.96 - 3.91 (m, 1H), 3.51 - 3.36 (m, 3H), 3.32 - 3.28 (m, 2H), 3.00 - 2.88 (m, 1H), 2.16 - 2.02 (m, 1H), 1.98 - 1.76 (m, 3H).

Example 210:

N-(3-chloro-4-fluoro-phenyl)-3-[3-(methoxymethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: preparation of tert-butyl 3-(methoxymethyl)pyrrolidine-1-carboxylate (compound 210b)

To a solution of tert-butyl 3-(hydroxymethyl)pyrrolidine-1-carboxylate (compound **210a**, 1.1 g, 5 mmol) in THF (30 mL) was added NaH (600 mg, 10 mmol, 60% oil dispersion) slowly at room temperature and followed by addition of methyl iodide (852 mg, 0.6 mmol). The reaction mixture was stirred at room temperature for 2 hours and then was quenched with water, extracted with EtOAc. The organic layer was dried and concentrated in *vacuo* to afford compound **210b** (1.2 g) as a slight yellow oil. LCMS ($M+H^+$): 216.

Step 2: preparation of 3-(methoxymethyl)pyrrolidine (compound 210c)

A solution of tert-butyl 3-(methoxymethyl)pyrrolidine-1-carboxylate (compound **210b**, 1.2 g, 5 mmol) in HCl/EA (30 mL) was stirred at room temperature for 2 hours. Then the reaction mixture was concentrated in *vacuo* to afford compound **210c** (1 g) as a slight yellow solid. LCMS ($M+H^+$): 116.

Step 3: preparation of tert-butyl 3-[3-(methoxymethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 210d)

To a mixture of 3-iodo-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **1e**, 175 mg 0.5 mmol), 3-(methoxymethyl)pyrrolidine (compound **210c**, 116 mg, 1.0 mmol), L-proline (23 mg, 0.2 mmol) and K_2CO_3 (207 mg, 1.5 mmol) in DMSO (5 mL) was added CuI (19 mg 0.1 mmol) under N_2. The resulting mixture was stirred in microwave for 2 hours at 120 °C, diluted with water, and extracted with EtOAc. The organic layer was concentrated. The residue was purified by column chromatography to afford compound **210d** (150 mg) as a slight yellow oil. LCMS ($M+H^+$): 337.

Step 4: preparation of 3-[3-(methoxymethyl)pyrrolidin-1-yl]-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound 210e)

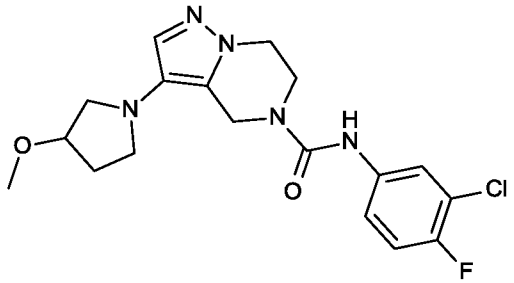
A solution of tert-butyl 3-[3-(methoxymethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **210d**, 70 mg, 0.3 mmol) in HCl/EA (10 mL) was stirred at room temperature for 2 hours. Then the reaction mixture was concentrated in *vacuo* to afford compound **210e** (60 mg) as a slight yellow solid. LCMS ($M+H^+$): 237.

Step 5: preparation of N-(3-chloro-4-fluoro-phenyl)-3-[3-(methoxymethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 210)

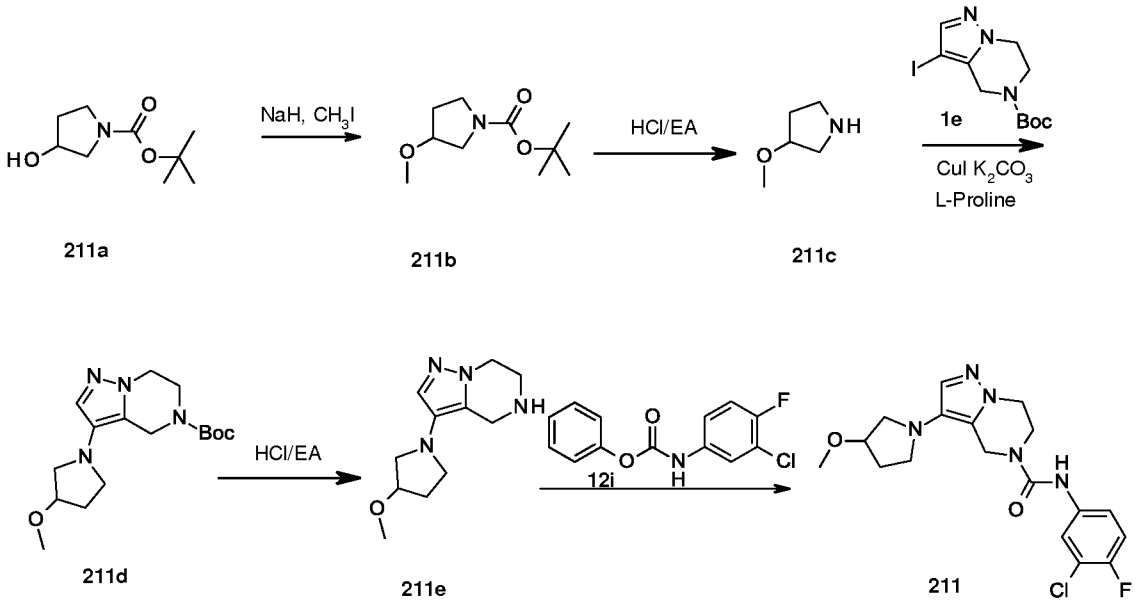
The title compound was prepared in analogy to the preparation of Example **140** by using phenyl N-(3-chloro-4-fluoro-phenyl)carbamate (compound **12i**) instead of phenyl N-(6-chloro-5-fluoro-2-pyridyl)carbamate (compound **140d**) and 3-[2-(methoxymethyl)pyrrolidin-1-yl]-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **210e**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **210** was obtained as a white solid (8 mg). LCMS ($M+H^+$): 408. ^1H NMR (400MHz, CD_3OD) δ ppm 7.62 (dd, *J*=2.6, 6.7 Hz, 1H), 7.36-7.32 (m, 1H), 7.21 (s, 1H), 7.17 (t, *J*=8.9 Hz, 1H), 4.83 (s, 2H), 4.18 (t, *J*=5.5 Hz, 2H), 4.00 (t, *J*=5.5 Hz, 2H), 3.43 (d, *J*=1.8 Hz, 2H), 3.41 (d, *J*=2.8 Hz, 2H), 3.38 (s, 3H), 3.35 (d, *J*=2.0 Hz, 1H), 3.24 (t, *J*=8.4 Hz, 1H), 3.18 - 3.09 (m, 1H), 2.92 (dd, *J*=6.0, 9.0 Hz, 1H), 2.62 - 2.57 (m, 1H), 2.17 - 2.05 (m, 1H), 1.72 -1.67 (m, 1H).

Example 211:

N-(3-chloro-4-fluoro-phenyl)-3-(3-methoxypyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of 3-(3-methoxypyrrolidin-1-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound 211e):

The compound **211e** was prepared in analogy to compound **210e** by using tert-butyl 3-hydroxypyrrolidine-1-carboxylate (compound **211a**, 1 g) instead of 3-(hydroxymethyl)pyrrolidine-1-carboxylate (compound **210a**). Compound **211e** was obtained as a slight yellow solid (60 mg). LCMS ($M+H^+$): 223.

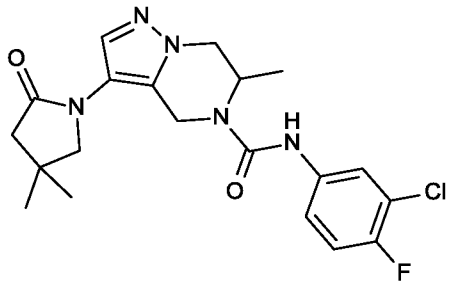
Preparation of N-(3-chloro-4-fluoro-phenyl)-3-(3-methoxypyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 211):

The title compound was prepared in analogy to the preparation of Example **140** by using phenyl N-(3-chloro-4-fluoro-phenyl)carbamate (compound **12i**) instead of phenyl N-(6-chloro-5-fluoro-2-pyridyl)carbamate (compound **140d**) and 3-(3-methoxypyrrolidin-1-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **211e**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **211** was obtained as a white solid (2 mg). LCMS ($M+H^+$): 394. ^1H NMR (400MHz, CD_3OD) δ ppm 7.63 (dd, *J*=2.6, 6.7 Hz, 1H), 7.36 -7.33 (m, 1H), 7.23 (s, 1H), 7.18 (t, *J*=9.0 Hz, 1H), 4.83 (s, 2H), 4.21 - 4.16 (m, 2H), 4.12 -

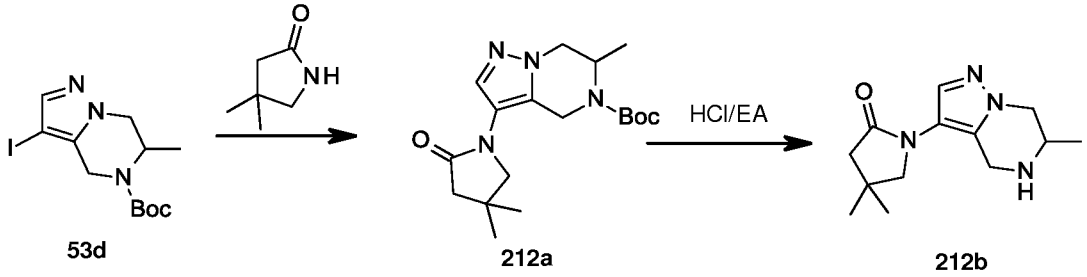
4.07 (m, 1H), 4.04 - 3.97 (m, 2H), 3.36 (s, 3H), 3.31 - 3.25 (m, 2H), 3.17 (dd, *J*=2.5, 10.3 Hz, 1H), 3.07 – 3.04 (m, 1H), 2.25 - 2.16 (m, 1H), 2.07 - 1.93 (m, 1H).

Example 212:

N-(3-chloro-4-fluoro-phenyl)-3-(4,4-dimethyl-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: **preparation of tert-butyl 3-(4,4-dimethyl-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 212a)**

To mixture of tert-butyl 3-iodo-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **53d**, 182 mg 0.5 mmol), 4,4-dimethylpyrrolidin-2-one (120 mg, 1.0 mmol), (1S,2S)-cyclohexane-1,2-diamine (23 mg, 0.2 mmol), CuI (19 mg 0.1 mmol) and K_3PO_4 (318 mg, 1.5 mmol) in DMSO (5 mL) under N_2 was stirred in microwave for 2 hours at 120 °C. The reaction mixture was diluted with water, extracted with EtOAc. The organic layer was concentrated to afford compound **212a** (150 mg) as a slight yellow oil. LCMS ($M+H^+$): 349.

Step 2: preparation of 4,4-dimethyl-1-(6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)pyrrolidin-2-one (compound 212b)

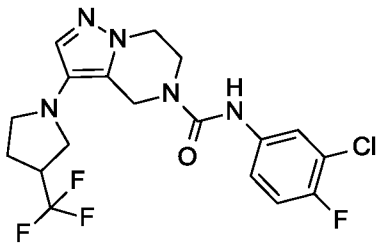
A solution of tert-butyl 3-(4,4-dimethyl-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **212a**, 150 mg, 0.4 mmol) in HCl/EA (15 mL) was stirred at room temperature for 2 hours. Then the reaction mixture was concentrated in *vacuo* to afford compound **212b** (120 mg) as a slight yellow solid. LCMS ($M+H^+$): 249.

Step 3: preparation of N-(3-chloro-4-fluoro-phenyl)-3-(4,4-dimethyl-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 212):

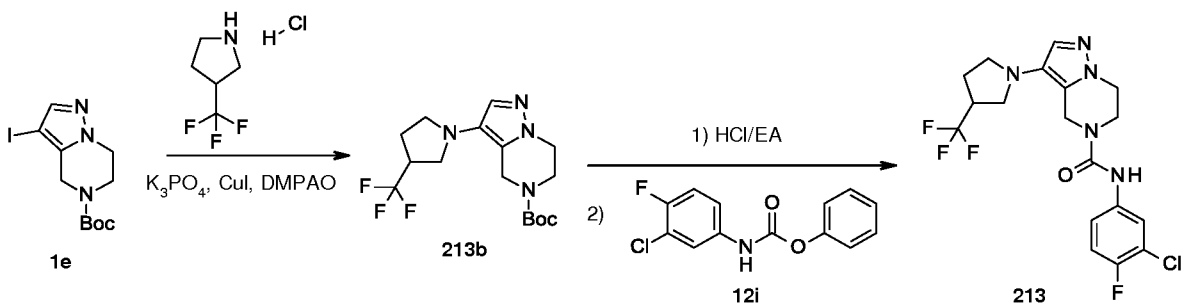
The title compound was prepared in analogy to the preparation of Example **140** by using phenyl N-(3-chloro-4-fluoro-phenyl)carbamate (compound **12i**) instead of phenyl N-(6-chloro-5-fluoro-2-pyridyl)carbamate (compound **140d**) and 4,4-dimethyl-1-(6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)pyrrolidin-2-one (compound **212b**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **212** was obtained as a white solid (10 mg). LCMS ($M+H^+$): 420. ^1H NMR (400MHz, CD_3OD) δ ppm 7.66 - 7.57 (m, 2H), 7.35 - 7.33 (m, 1H), 7.17 (t, *J*=8.9 Hz, 1H), 5.04 (d, *J*=16.8 Hz, 1H), 4.99 - 4.93 (m, 1H), 4.51 (d, *J*=16.8 Hz, 1H), 4.30 (dd, *J*=4.4, 12.7 Hz, 1H), 4.19 - 4.16 (m, 1H), 3.67 - 3.51 (m, 2H), 2.41 (s, 2H), 1.36 - 1.17 (m, 9H).

Example 213:

N-(3-chloro-4-fluoro-phenyl)-3-[3-(trifluoromethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:

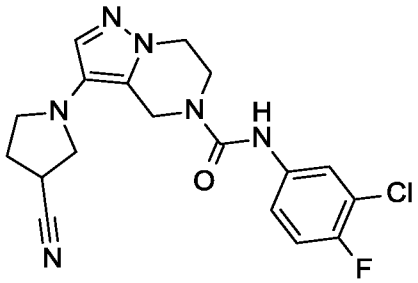


Preparation of N-(3-chloro-4-fluoro-phenyl)-3-[3-(trifluoromethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 213):

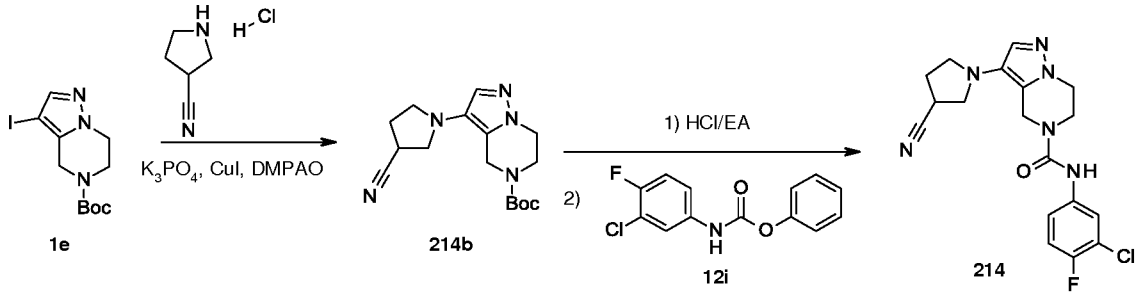
The title compound was prepared in analogy to Example **168** by using 3-(trifluoromethyl)pyrrolidine hydrochloride instead of 2-methylpyrrolidine hydrochloride. Example **213** was obtained as a solid (5.0 mg). LCMS ($M+H^+$): 432. ^{1}H NMR (400MHz, chloroform-d) δ ppm 7.55 (dd, *J*=2.6, 6.4 Hz, 1H), 7.25 - 7.19 (m, 2H), 7.12 (d, *J*=8.5 Hz, 1H), 4.74 (s, 2H), 4.26 (t, *J*=5.4 Hz, 2H), 4.01 - 3.94 (m, 2H), 3.34 (s, 1H), 3.18 (s, 3H), 3.04 (d, *J*=9.5 Hz, 1H), 2.30 - 2.20 (m, 1H), 2.17 - 2.08 (m, 1H).

Example 214:

N-(3-chloro-4-fluoro-phenyl)-3-(3-cyanopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:

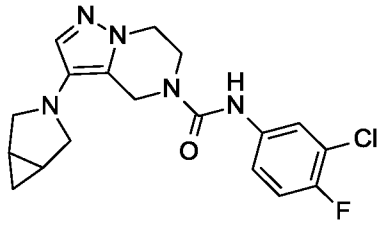


Preparation of N-(3-chloro-4-fluoro-phenyl)-3-(3-cyanopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 214):

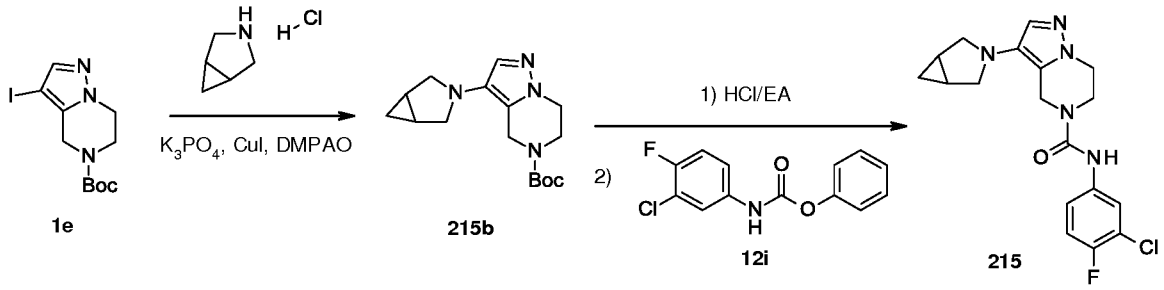
The title compound was prepared in analogy to Example **168** by using pyrrolidine-3-carbonitrile hydrochloride instead of 2-methylpyrrolidine hydrochloride. Example **214** was obtained as a solid (7.2 mg). LCMS ($M+H^+$): 389. ^{1}H NMR (400MHz, chloroform-d) δ ppm 7.54 (dd, *J*=2.6, 6.4 Hz, 1H), 7.27 - 7.20 (m, 2H), 7.13 - 7.04 (m, 1H), 6.72 (s, 1H), 4.79 - 4.68 (m, 2H), 4.25 (t, *J*=5.4 Hz, 2H), 4.03 - 3.94 (m, 2H), 3.40 - 3.34 (m, 2H), 3.33 - 3.26 (m, 1H), 3.25 - 3.11 (m, 2H), 2.47 - 2.25 (m, 2H).

Example 215:

3-[3-azabicyclo[3.1.0]hexan-3-yl]-N-(3-chloro-4-fluoro-phenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:

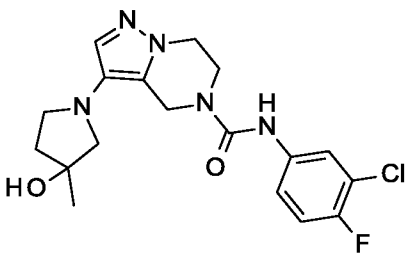


Preparation of 3-[3-azabicyclo[3.1.0]hexan-3-yl]-N-(3-chloro-4-fluoro-phenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 215):

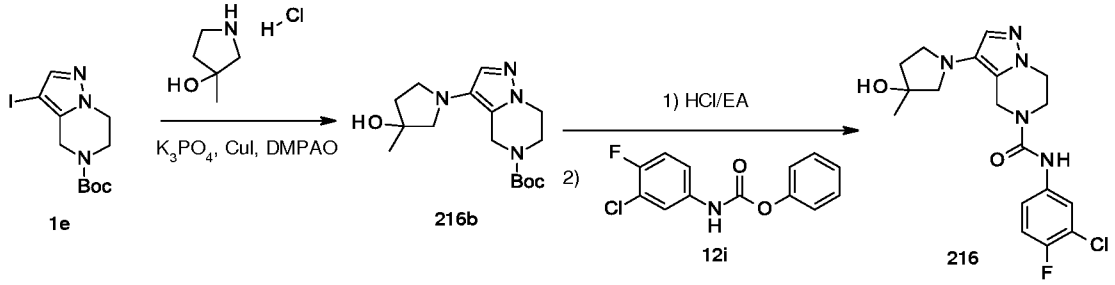
The title compound was prepared in analogy to Example **168** by using 3-azabicyclo[3.1.0]hexane hydrochloride instead of 2-methylpyrrolidine hydrochloride. Example **215** was obtained as a solid (2.4 mg). LCMS ($M+H^+$): 376. ^1H NMR (400MHz, CD_3OD) δ ppm 7.62 (dd, *J*=2.6, 6.7 Hz, 1H), 7.34 (ddd, *J*=2.6, 4.2, 9.0 Hz, 1H), 7.24 - 7.08 (m, 2H), 4.80 (s, 2H), 4.21 - 4.12 (m, 2H), 4.04 - 3.94 (m, 2H), 3.42 (d, *J*=8.0 Hz, 2H), 3.02 (d, *J*=7.8 Hz, 2H), 1.63 - 1.53 (m, 2H), 0.68 (q, *J*=4.0 Hz, 1H), 0.57 (dt, *J*=4.4, 7.7 Hz, 1H).

Example 216:

N-(3-chloro-4-fluoro-phenyl)-3-(3-hydroxy-3-methyl-pyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:

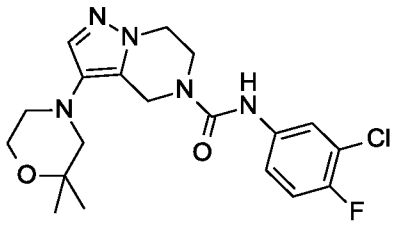


Preparation of N-(3-chloro-4-fluoro-phenyl)-3-(3-hydroxy-3-methyl-pyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 216):

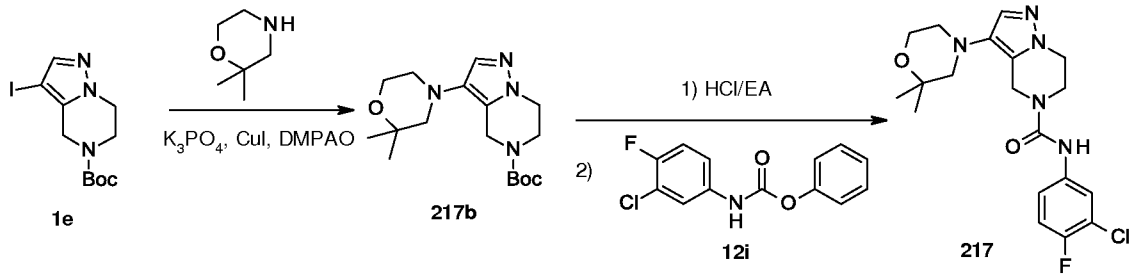
The title compound was prepared in analogy to Example **168** by using 3-methylpyrrolidin-3-ol hydrochloride instead of 2-methylpyrrolidine hydrochloride. Example **216** was obtained as a solid (0.5 mg). LCMS ($M+H^+$): 394. ^1H NMR (400MHz, CD_3OD) δ ppm 7.62 (dd, *J*=2.5, 6.5 Hz, 1H), 7.38 - 7.31 (m, 1H), 7.22 - 7.17 (m, 2H), 4.84 (s, 2H), 4.22 - 4.14 (m, 2H), 4.04 - 3.97 (m, 2H), 3.46 - 3.35 (m, 2H), 3.21 - 3.14 (m, 2H), 2.05 - 1.97 (m, 2H), 1.45 (s, 3H).

Example 217:

N-(3-chloro-4-fluoro-phenyl)-3-(2,2-dimethylmorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



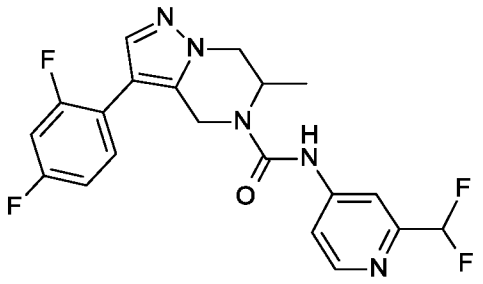
Preparation of N-(3-chloro-4-fluoro-phenyl)-3-(2,2-dimethylmorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 217):

The title compound was prepared in analogy to Example **168** by using 2,2-dimethylmorpholine instead of 2-methylpyrrolidine hydrochloride. Example **217** was obtained as a solid (12.2 mg). LCMS ($M+H^+$): 408. ^1H NMR (400MHz, CD_3OD) δ ppm 7.62 (dd, *J*=2.6,

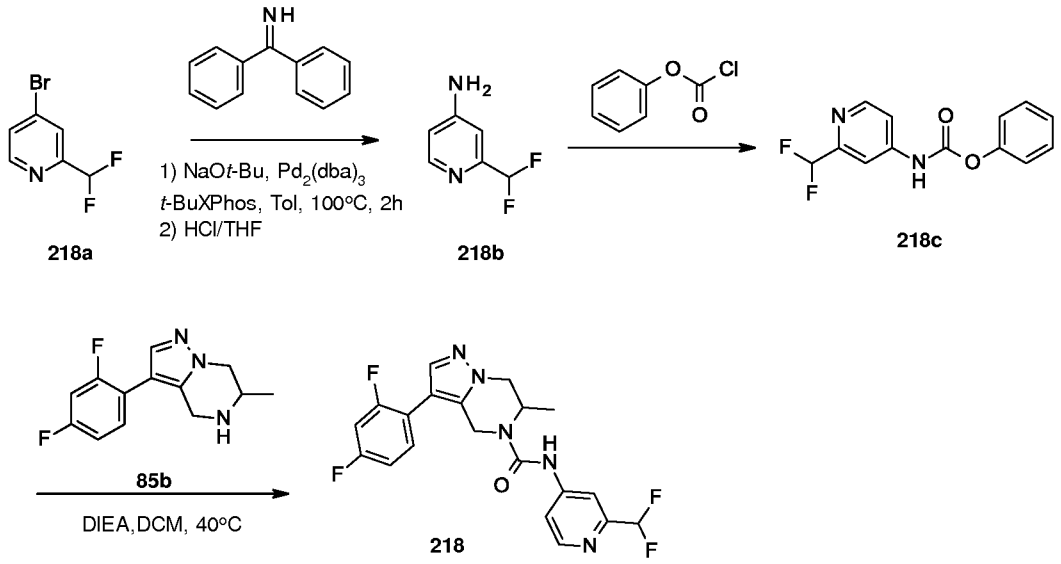
6.7 Hz, 1H), 7.38 - 7.31 (m, 2H), 7.18 (t, *J*=8.9 Hz, 1H), 4.74 (s, 2H), 4.22 - 4.16 (m, 2H), 4.06 - 3.96 (m, 2H), 3.88 - 3.83 (m, 2H), 2.88 - 2.83 (m, 2H), 2.71 (s, 2H), 1.34 (s, 6H).

Example 218:

N-[2-(difluoromethyl)-4-pyridyl]-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (218c):

The compound **218c** was prepared in analogy to compound **147c** by using 4-bromo-2-(difluoromethyl)pyridine instead of 1-bromo-3-(1,1-difluoroethyl)benzene (compound **147a**). Compound **218c** was obtained as a yellow solid (264 mg). LCMS ($M-H^+$): 263.

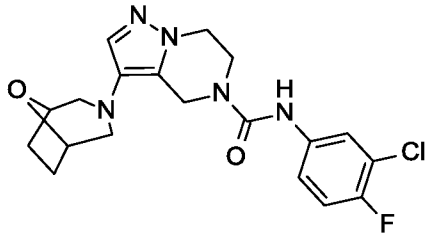
Preparation of N-[2-(difluoromethyl)-4-pyridyl]-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 218):

The title compound was prepared in analogy to Example **12** by using 3-(2,4-difluorophenyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **85b**) instead of

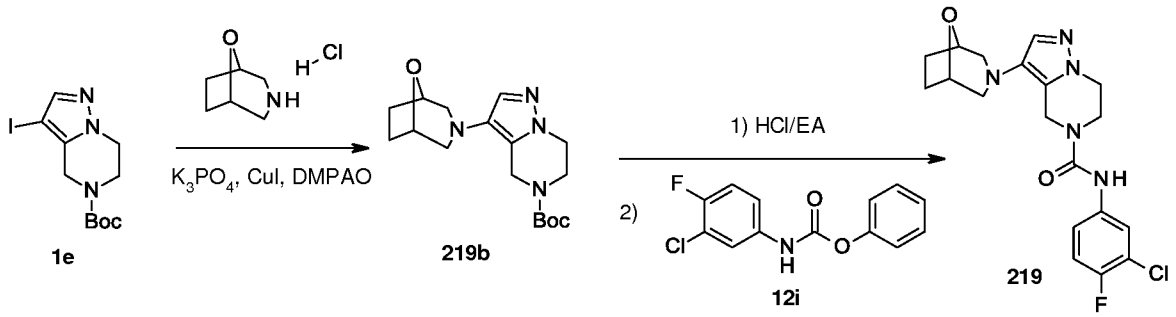
8-(4-fluorophenyl)-1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazine (compound **12h**) and phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**) instead of phenyl N-(3-chloro-4-fluoro-phenyl)carbamate (compound **12i**). Example **218** was obtained as a solid (30.3 mg). LCMS ($M+H^+$): 420. ^1H NMR (400MHz, CD_3OD) δ ppm 8.41 (d, *J*=5.8 Hz, 1H), 7.87 (d, *J*=2.3 Hz, 1H), 7.74 (d, *J*=1.5 Hz, 1H), 7.66 (dd, *J*=2.0, 5.8 Hz, 1H), 7.55 - 7.48 (m, 1H), 7.14 - 7.05 (m, 2H), 6.82 - 6.50 (m, 1H), 5.16 (d, *J*=16.8 Hz, 1H), 5.08 - 5.01 (m, 1H), 4.65 (d, *J*=16.8 Hz, 1H), 4.40 (dd, *J*=4.4, 12.9 Hz, 1H), 4.29 - 4.24 (m, 1H), 1.32 (d, *J*=6.8 Hz, 3H).

Example 219:

N-(3-chloro-4-fluoro-phenyl)-3-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:

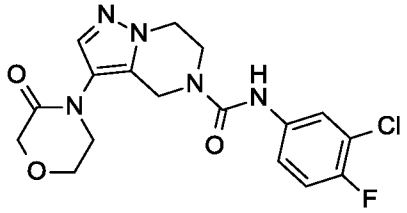


Preparation of N-(3-chloro-4-fluoro-phenyl)-3-[8-oxa-3-azabicyclo[3.2.1]octan-3-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 219):

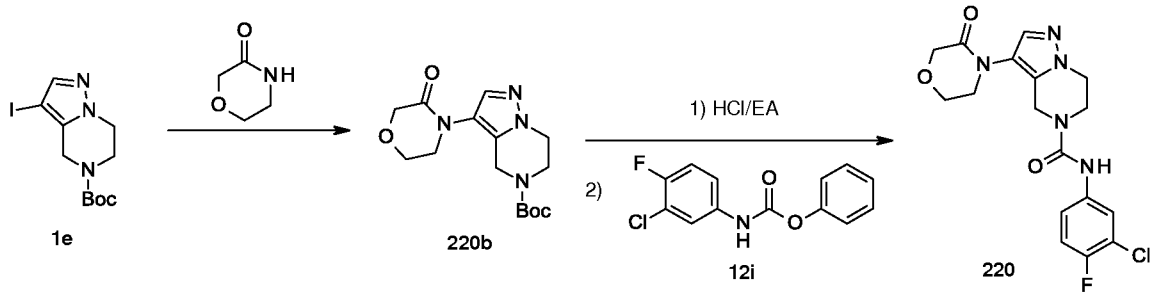
The title compound was prepared in analogy to Example **168** by using 8-oxa-3-azabicyclo[3.2.1]octane hydrochloride instead of 2-methylpyrrolidine hydrochloride. Example **219** was obtained as a solid (6.4 mg). LCMS ($M+H^+$): 406. ^1H NMR (400MHz, chloroform-d) δ ppm 7.52 (dd, *J*=2.6, 6.4 Hz, 1H), 7.29 (s, 1H), 7.21 (dd, *J*=2.9, 3.9 Hz, 1H), 7.13 - 7.07 (m, 1H), 6.57 (s, 1H), 4.67 (s, 2H), 4.44 - 4.36 (m, 2H), 4.28 - 4.20 (m, 2H), 3.95 (t, *J*=5.4 Hz, 2H), 3.06 - 2.98 (m, 2H), 2.81 (d, *J*=11.0 Hz, 2H), 2.08 - 1.97 (m, 4H).

Example 220:

N-(3-chloro-4-fluoro-phenyl)-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: preparation of tert-butyl 3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 220b)

To a mixture of morpholin-3-one (24 mg, 0.24 mmol), tert-butyl 3-iodo-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **1e**, 70 mg, 0.20 mmol), K_3PO_4 (85 mg, 0.40 mmol), CuI (7.6 mg, 40 μmol) and (1R,2R)-N1,N2-dimethylcyclohexane-1,2-diamine (5.7 mg, 40 μmol) was suspended in DMSO (5.0 mL). The reaction mixture was flushed with nitrogen and sealed. Then the reaction mixture was stirred at 105 °C in microwave for 2 hours. The reaction mixture was diluted with ethyl acetate, washed with water. The organic layer was concentrated to give crude compound **220b** (65 mg). LCMS ($M+H^+$): 323.

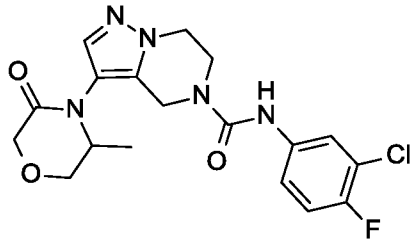
Step 2: preparation of N-(3-chloro-4-fluoro-phenyl)-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 220)

A solution of tert-butyl 3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **220b**, 129 mg, 0.40 mmol) in HCl/EA (1N, 5.0 mL) was stirred at room temperature overnight. Petroleum ether (45 mL) was added. The reaction mixture was centrifuged, and a yellowish solid was collected. The obtained solid was dissolved in DCM (3.0 mL), to which DIPEA (0.4 mL) and phenyl N-(3-chloro-4-fluoro-phenyl)carbamate (128 mg, 0.48 mmol) were added. The reaction mixture was stirred at 40 °C for 3 hours. The reaction mixture was concentrated in *vacuo* to give crude product, which was purified by preparative HPLC to afford Example **220** (61 mg). LCMS ($M+H^+$): 394. ^1H NMR (400MHz, chloroform-d)

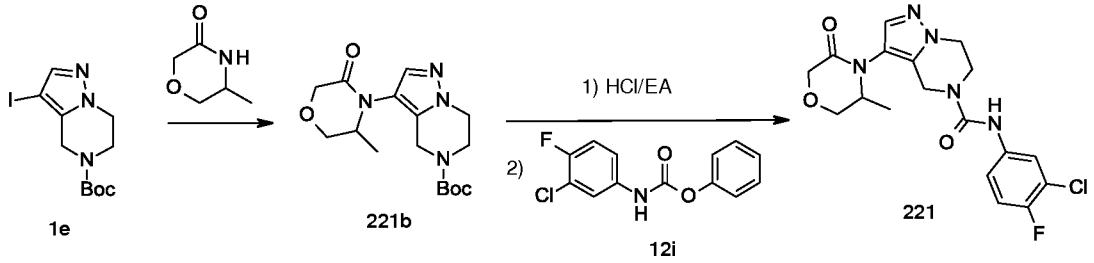
δ ppm 7.85 (s, 1H), 7.65 (dd, *J*=2.5, 6.5 Hz, 1H), 7.50 (s, 1H), 7.35 - 7.30 (m, 1H), 7.05 (t, *J*=8.8 Hz, 1H), 4.61 (s, 2H), 4.39 (s, 2H), 4.27 - 4.20 (m, 2H), 4.13 - 4.05 (m, 4H), 3.86 - 3.81 (m, 2H).

Example 221:

N-(3-chloro-4-fluoro-phenyl)-3-(3-methyl-5-oxo-morpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:

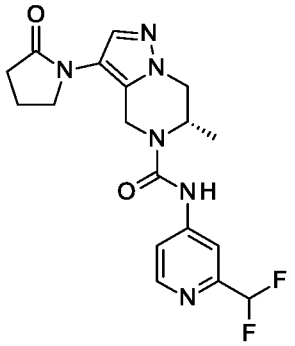


Preparation of N-(3-chloro-4-fluoro-phenyl)-3-(3-methyl-5-oxo-morpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 221):

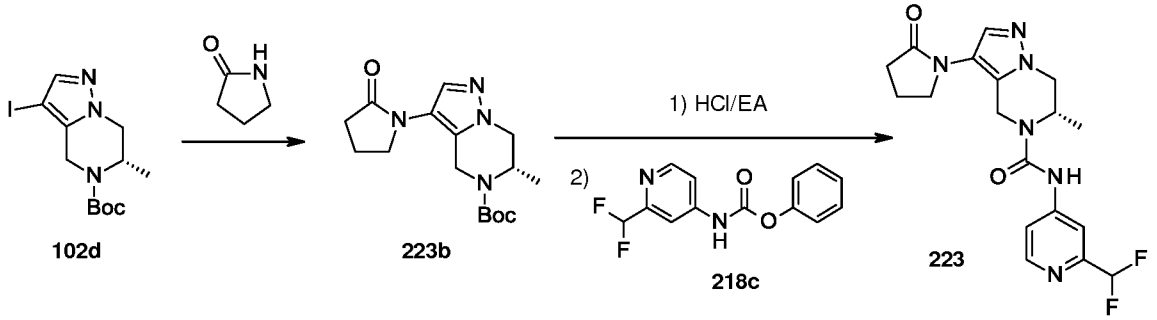
The title compound was prepared in analogy to Example **220** by using 5-methylmorpholin-3-one instead of morpholin-3-one. Example **221** was obtained as a solid (24.5 mg). LCMS ($M+H^+$): 408. ^{1}H NMR (400MHz, chloroform-d) δ ppm 7.83 (s, 1H), 7.64 (dd, *J*=2.6, 6.7 Hz, 1H), 7.47 (s, 1H), 7.35 - 7.29 (m, 1H), 7.04 (t, *J*=8.9 Hz, 1H), 4.83 - 4.76 (m, 1H), 4.52 - 4.45 (m, 1H), 4.42 - 4.33 (m, 2H), 4.32 (s, 1H), 4.32 - 4.26 (m, 1H), 4.26 - 4.20 (m, 2H), 4.11 (dd, *J*=3.5, 11.8 Hz, 1H), 4.03 - 3.97 (m, 1H), 3.80 (dd, *J*=4.1, 11.9 Hz, 1H), 3.77 - 3.69 (m, 1H), 1.28 (d, *J*=6.3 Hz, 3H).

Example 223:

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: preparation of tert-butyl (6S)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 223b)

To a mixture of pyrrolidin-2-one (102 mg, 1.2 mmol), tert-butyl (6S)-3-iodo-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **102d**, 363 mg, 1.0 mmol), K_3PO_4 (424 mg, 2.0 mmol), CuI (38.1 mg, 200 μmol) and (1R,2R)-N1,N2-dimethylcyclohexane-1,2-diamine (28.4 mg, 200 μmol) was suspended in DMSO (5.0 mL). The reaction mixture was flushed with nitrogen and sealed. Then the reaction mixture was stirred at 105 °C in microwave for 2 hours. The reaction mixture was diluted with ethyl acetate, and washed with water. The organic layer was concentrated to give crude compound **223b** (320 mg). LCMS ($M+H^+$): 321.

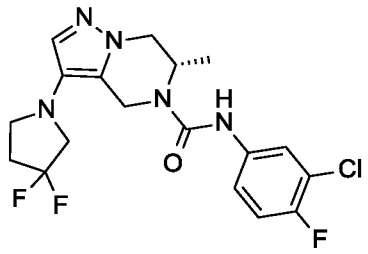
Step 2: preparation of (6S)-N-[2-(difluoromethyl)-4-pyridyl]-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 223)

A solution of tert-butyl (6S)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **223b**, 64 mg, 0.20 mmol) in HCl/EA (1N, 5.0 mL) was stirred at room temperature overnight. Petroleum ether (45 mL) was added. The reaction mixture was centrifuged, and a yellowish solid was collected. The obtained solid was dissolved in DCM (3.0 mL), to which DIPEA (0.4 mL) and phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**, 63.4 mg, 0.24 mmol) were added. The reaction mixture was stirred at 40 °C for 3 hours. The reaction mixture was concentrated in *vacuo* to give crude product, which was purified by preparative HPLC to afford Example **223** (11.3 mg). LCMS

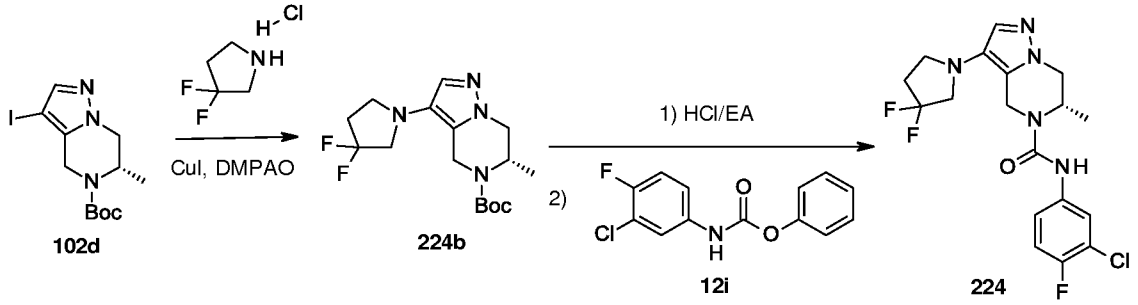
(M+H$^+$): 391. ^{1}H NMR (400MHz, chloroform-d) δ ppm 8.51 (s, 1H), 8.46 (d, *J*=5.8 Hz, 1H), 7.82 (d, *J*=2.0 Hz, 1H), 7.65 (d, *J*=5.5 Hz, 1H), 7.42 (s, 1H), 6.75 - 6.42 (m, 1H), 5.21 (d, *J*=16.8 Hz, 1H), 5.11 - 5.03 (m, 1H), 4.37 (d, *J*=16.8 Hz, 1H), 4.34 - 4.29 (m, 1H), 4.05 - 3.93 (m, 2H), 3.85 - 3.75 (m, 1H), 2.69 - 2.60 (m, 2H), 2.34 - 2.23 (m, 2H), 1.43 (d, *J*=6.8 Hz, 3H).

Example 224:

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(3,3-difluoropyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:

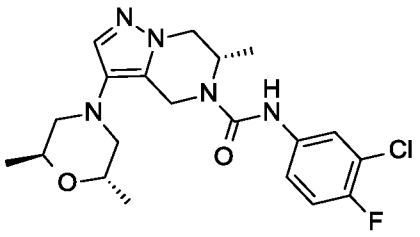


Preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-3-(3,3-difluoropyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 224):

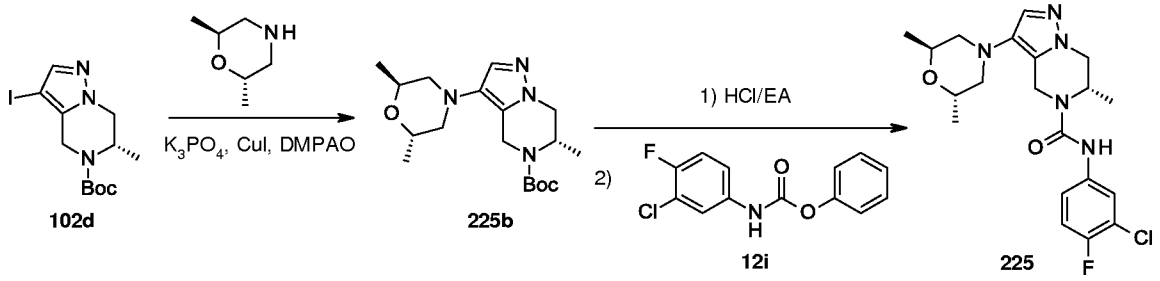
The title compound was prepared in analogy to Example **168** by using 3,3-difluoropyrrolidine hydrochloride instead of 2-methylpyrrolidine hydrochloride. Example **224** was obtained as a solid (14.4 mg). LCMS (M+H$^+$): 414. ^{1}H NMR (400MHz, chloroform-d) δ ppm 7.57 (dd, *J*=2.8, 6.5 Hz, 1H), 7.28 - 7.21 (m, 2H), 7.14 - 7.08 (m, 1H), 6.48 (s, 1H), 4.88 (d, *J*=15.3 Hz, 2H), 4.51 (d, *J*=15.1 Hz, 1H), 4.30 (dd, *J*=4.1, 12.7 Hz, 1H), 4.18 - 4.11 (m, 1H), 3.46 (t, *J*=13.2 Hz, 2H), 3.31 (t, *J*=7.0 Hz, 2H), 2.52 - 2.39 (m, 2H), 1.26 (d, *J*=6.8 Hz, 3H).

Example 225:

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-[trans-2,6-dimethylmorpholin-4-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:

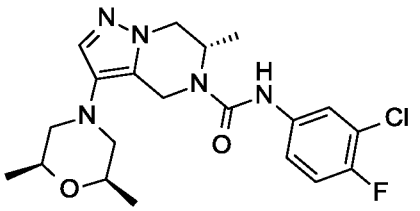


Preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-3-[trans-2,6-dimethylmorpholin-4-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 225):

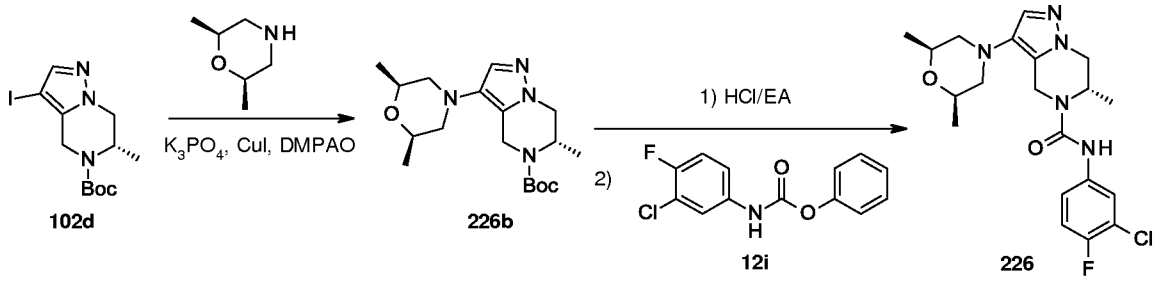
The title compound was prepared in analogy to Example **168** by using *trans*-2,6-dimethylmorpholine instead of 2-methylpyrrolidine hydrochloride. Example **225** was obtained as a solid (25.8 mg). LCMS ($M+H^+$): 422. ^{1}H NMR (400MHz, chloroform-d) δ ppm 7.56 (dd, *J*=2.5, 6.5 Hz, 1H), 7.36 (d, *J*=6.3 Hz, 1H), 7.26 - 7.18 (m, 1H), 7.16 - 7.07 (m, 1H), 6.38 (s, 1H), 4.89 - 4.78 (m, 2H), 4.46 (dd, *J*=6.7, 15.4 Hz, 1H), 4.30 (dd, *J*=4.3, 12.8 Hz, 1H), 4.19 - 4.11 (m, 3H), 2.96 (dd, *J*=3.3, 11.0 Hz, 2H), 2.65 - 2.58 (m, 2H), 1.34 (d, *J*=6.5 Hz, 6H), 1.27 (dd, *J*=1.5, 6.8 Hz, 3H).

Example 226:

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-[cis-2,6-dimethylmorpholin-4-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:

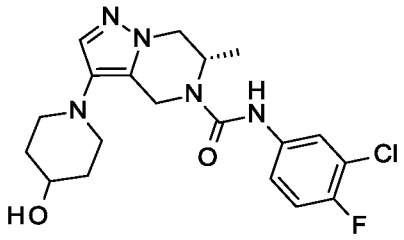


Preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-3-[cis-2,6-dimethylmorpholin-4-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 226):

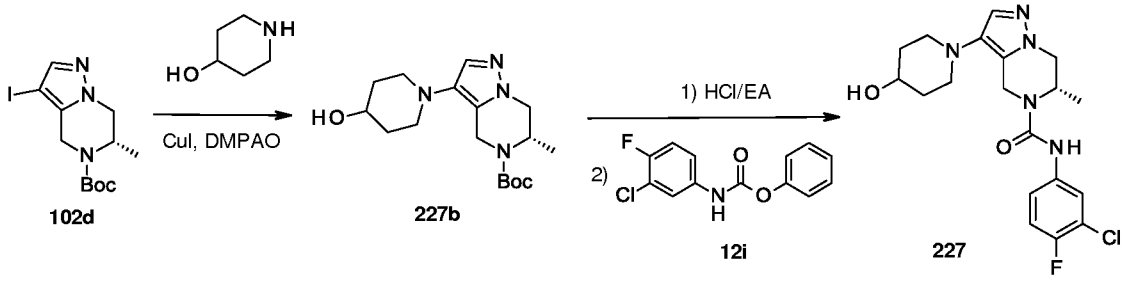
The title compound was prepared in analogy to Example **168** by using *cis*-2,6-dimethylmorpholine instead of 2-methylpyrrolidine hydrochloride. Example **226** was obtained as a solid (34.0 mg). LCMS ($M+H^+$): 422. ^{1}H NMR (400MHz, chloroform-d) δ ppm 7.55 (dd, *J*=2.6, 6.4 Hz, 1H), 7.36 (s, 1H), 7.27 - 7.21 (m, 1H), 7.10 (t, *J*=8.5 Hz, 1H), 6.51 (s, 1H), 4.93 - 4.85 (m, 1H), 4.82 (d, *J*=15.3 Hz, 1H), 4.48 (d, *J*=15.3 Hz, 1H), 4.29 (dd, *J*=4.3, 12.8 Hz, 1H), 4.18 - 4.11 (m, 1H), 3.87 - 3.78 (m, 2H), 2.97 - 2.90 (m, 2H), 2.48 - 2.40 (m, 2H), 1.27 - 1.20 (m, 9H).

Example 227:

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-hydroxy-1-piperidyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:

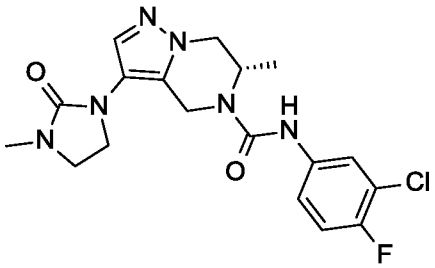


Preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-hydroxy-1-piperidyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 227):

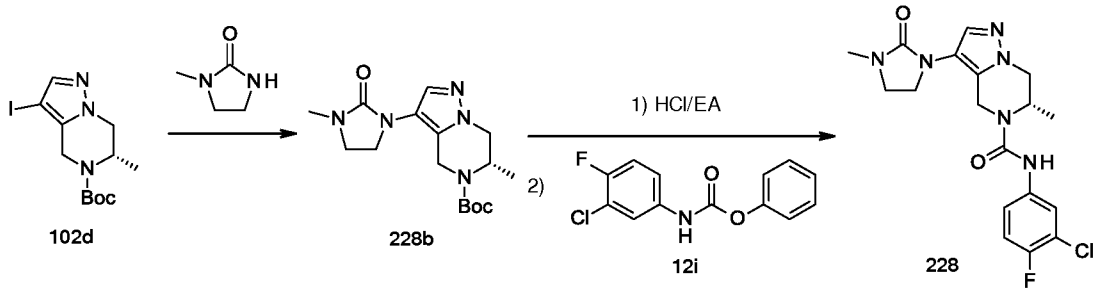
The title compound was prepared in analogy to Example **168** by using piperidin-4-ol instead of 2-methylpyrrolidine hydrochloride. Example **227** was obtained as a solid (31.3 mg). LCMS ($M+H^+$): 408. ^1H NMR (400MHz, chloroform-d) δ ppm 7.58 (dd, *J*=2.6, 6.4 Hz, 1H), 7.38 (s, 1H), 7.27 - 7.21 (m, 1H), 7.11 (t, *J*=8.7 Hz, 1H), 6.55 (br. s., 1H), 4.98 - 4.89 (m, 1H), 4.82 (d, *J*=15.3 Hz, 1H), 4.49 (d, *J*=15.3 Hz, 1H), 4.29 (dd, *J*=4.3, 12.8 Hz, 1H), 4.14 (dd, *J*=1.1, 12.7 Hz, 1H), 3.90 - 3.82 (m, 1H), 3.14 (dd, *J*=4.6, 11.2 Hz, 2H), 2.78 (t, *J*=9.9 Hz, 2H), 2.02 (d, *J*=9.3 Hz, 2H), 1.79 - 1.67 (m, 4H), 1.24 (d, *J*=7.0 Hz, 3H).

Example 228:

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(3-methyl-2-oxo-imidazolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



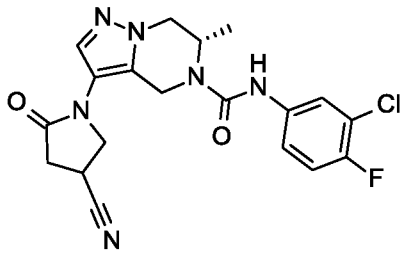
Preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(3-methyl-2-oxo-imidazolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 228):

The title compound was prepared in analogy to Example **220** by using 1-methylimidazolidin-2-one instead of morpholin-3-one and tert-butyl (6S)-3-iodo-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **102d**) instead of tert-butyl 3-iodo-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **1e**). Example **228** was obtained as a solid (15.1 mg). LCMS ($M+H^+$): 407. ^1H NMR (400MHz, chloroform-d) δ ppm 7.89 (s, 1H), 7.68 (dd, *J*=2.6, 6.7 Hz, 1H), 7.42 - 7.35 (m, 2H), 7.05 (t, *J*=8.9 Hz, 1H), 5.17 (d, *J*=16.6 Hz, 1H), 5.08 (t, *J*=7.2 Hz, 1H), 4.41 (d, *J*=16.6 Hz, 1H), 4.29 (dd, *J*=5.5, 12.8 Hz, 1H),

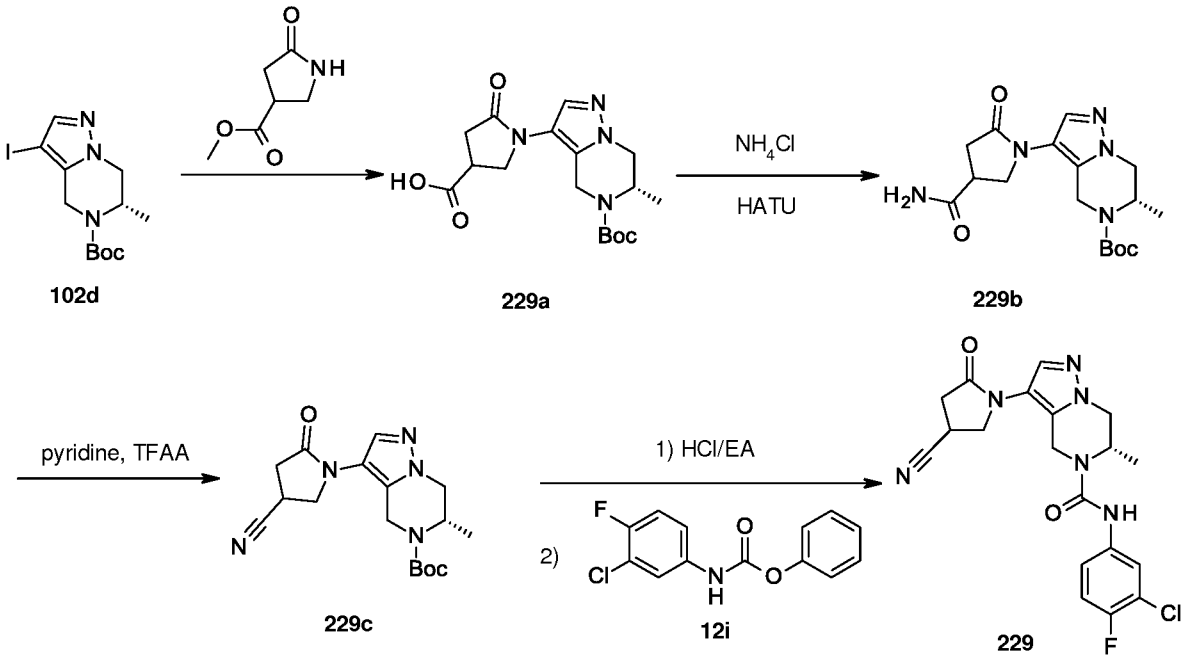
4.04 - 3.98 (m, 1H), 3.87 (d, *J*=8.8 Hz, 1H), 3.72 (d, *J*=6.3 Hz, 1H), 3.60 - 3.52 (m, 2H), 2.93 (s, 3H), 1.39 (d, *J*=7.0 Hz, 3H).

Example 229:

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-cyano-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: **preparation of 1-[(6S)-5-tert-butoxycarbonyl-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-5-oxo-pyrrolidine-3-carboxylic acid (compound 229a)**

A mixture of tert-butyl (6S)-3-iodo-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **102d**, 364 mg, 1.0 mmol), methyl 5-oxopyrrolidine-3-carboxylate (286 mg, 2.0 mmol), (1S,2S)-cyclohexane-1,2-diamine (46 mg, 0.4 mmol), CuI (38 mg 0.2 mmol) and K_3PO_4 (636 mg, 3 mmol) in DMSO (10 mL) under N_2 was stirred at microwave for 2 hours at 120 °C. The reaction mixture was diluted with hydrochloride acid (0.5 M, 10 mL), extracted with

EtOAc (20 mL) twice. The organic layer was concentrated to afford compound **229a** (200 mg) as a slight yellow solid. LCMS ($M+H^+$): 365.

Step 2: preparation of tert-butyl (6S)-3-(4-carbamoyl-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 229b)

A mixture of 1-[(6S)-5-tert-butoxycarbonyl-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-5-oxo-pyrrolidine-3-carboxylic acid (compound **229a**, 183 mg, 0.5 mmol), HATU (210 mg, 0.6 mmol), NH_4Cl (138 mg, 2.5 mmol) and DIPEA (770 mg, 6 mmol) in THF (10 mL) was stirred at 60 °C for 2 hours. The reaction mixture was diluted with hydrochloride acid (0.5 M, 15 mL), and extracted with EtOAc (20 mL) twice. The organic layer was concentrated to afford compound **229b** (150 mg) as a slight yellow solid. LCMS ($M+H^+$): 364.

Step 3: preparation of tert-butyl (6S)-3-(4-cyano-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 229c)

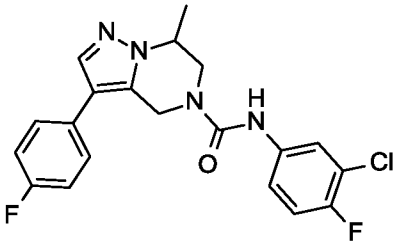
To a solution of tert-butyl (6S)-3-(4-carbamoyl-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **229b**, 150 mg, 0.41 mmol) in dry tetrahydrofuran (5.0 mL) at 0 °C under nitrogen was added pyridine (0.5 mL, 6.2 mmol) followed by dropwise addition of a solution of trifluoroacetic anhydride (0.5 mL, 3.5 mmol) in dry tetrahydrofuran (1.0 mL). The resulting reaction mixture was allowed to warm slowly to room temperature, and stirred overnight, then quenched with ice-water, and extracted with EtOAc (20 mL) twice. The organic layer was concentrated to afford compound **229c** (138 mg) as a slight yellow solid. LCMS ($M+H^+$): 346.

Step 4: preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-cyano-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 229)

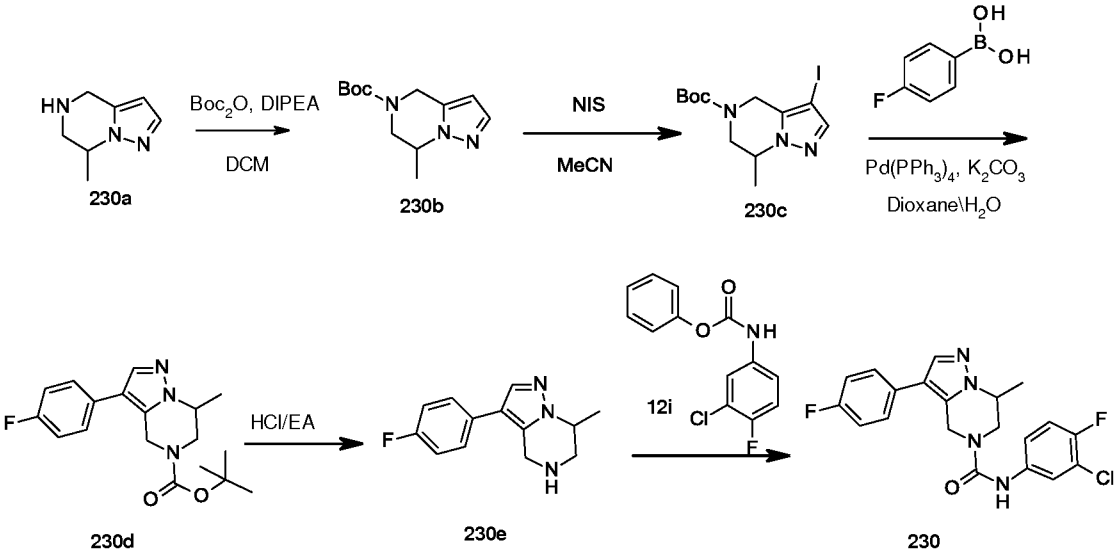
The title compound was prepared in analogy to Example **220** by using tert-butyl (6S)-3-(4-cyano-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **229c**) instead of tert-butyl 3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **220b**). Example **229** was obtained as a solid (29.4 mg). LCMS ($M+H^+$): 417. ^1H NMR (400MHz, chloroform-d) δ ppm 7.65 - 7.58 (m, 1H), 7.45 (d, *J*=9.0 Hz, 1H), 7.33 - 7.29 (m, 1H), 7.26 - 7.18 (m, 1H), 7.07 (dt, *J*=1.0, 8.8 Hz, 1H), 5.15 - 4.96 (m, 2H), 4.43 (m, 1H), 4.31 (m, 1H), 4.22 (dd, *J*=8.0, 10.0 Hz, 0.5H), 4.15 - 4.05 (m, 2H), 4.03 (dd, *J*=5.1, 10.2 Hz, 0.5H), 3.63 - 3.53 (m, 1H), 3.07 - 2.90 (m, 2H), 1.36 (m, 3H).

Example 230:

N-(3-chloro-4-fluoro-phenyl)-3-(4-fluorophenyl)-7-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of 3-(4-fluorophenyl)-7-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound 230e):

The compound **230e** was prepared in analogy to compound **9e** by using 7-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **230a**, catalog number: PBCS1406244, PharmBlock(Nanjing) R&D Co. Ltd.) instead of 5,6,7,8-tetrahydroimidazo[1,5-a]pyrazine (compound **9a**). Compound **230e** was obtained as a white solid (250 mg). LCMS ($M+H^+$): 232.

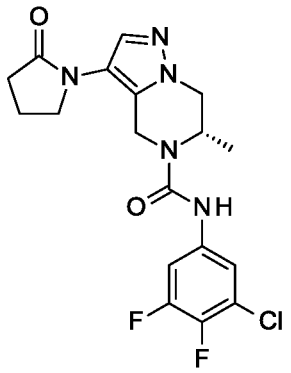
Preparation of N-(3-chloro-4-fluoro-phenyl)-3-(4-fluorophenyl)-7-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 230):

The title compound was prepared in analogy to the preparation of Example **140** by using phenyl N-(3-chloro-4-fluoro-phenyl)carbamate (compound **12i**) instead of phenyl N-(6-chloro-5-fluoro-2-pyridyl)carbamate (compound **140d**) and 3-(4-fluorophenyl)-7-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **230e**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **230** was obtained as a white solid (21 mg). LCMS ($M+H^+$): 403. ^1H NMR (400MHz, CD_3OD) δ ppm 7.77 (s, 1H), 7.61 (dd, *J*=2.6, 6.7 Hz, 1H), 7.49 (dd, *J*=5.3, 9.0 Hz, 2H), 7.33 - 7.31 (m, 1H), 7.22 - 7.12 (m, 3H), 4.98 (s, 2H),

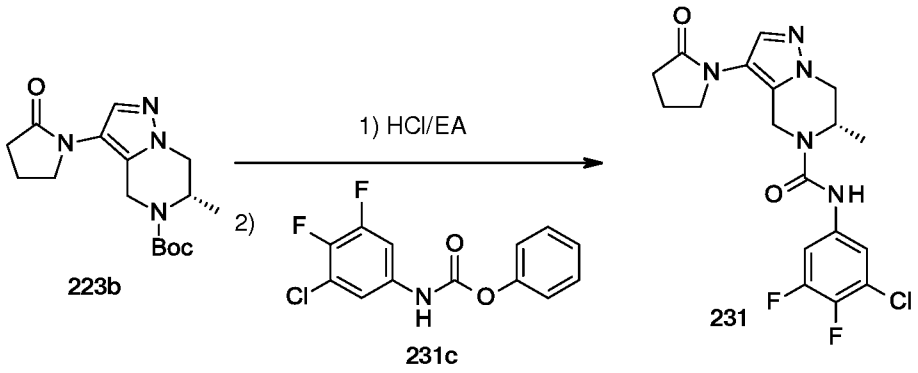
4.52 - 4.48 (m, 1H), 4.09 (dd, *J*=4.0, 14.1 Hz, 1H), 3.88 (dd, *J*=6.1, 13.9 Hz, 1H), 1.59 (d, *J*=6.5 Hz, 3H).

Example 231:

(6S)-N-(3-chloro-4,5-difluoro-phenyl)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



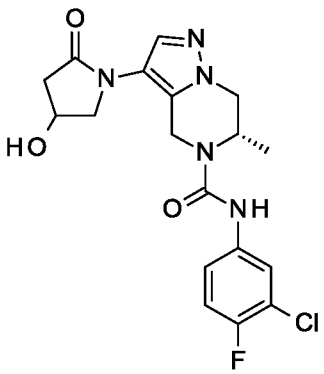
Preparation of (6S)-N-(3-chloro-4,5-difluoro-phenyl)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 231):

The title compound was prepared in analogy to Example **223** by using phenyl N-(3-chloro-4,5-difluoro-phenyl)carbamate (compound **231c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). Example **231** was obtained as a solid (24.0 mg). LCMS ($M+H^+$): 410. ^1H NMR (400MHz, chloroform-d) δ ppm 8.04 (s, 1H), 7.46 - 7.37 (m, 3H), 5.13 (d, *J*=17.1 Hz, 1H), 5.09 - 5.02 (m, 1H), 4.36 - 4.27 (m, 2H), 4.03 - 3.94 (m, 2H), 3.77 (ddd, *J*=5.4, 7.9, 9.5 Hz, 1H), 2.70 - 2.57 (m, 2H), 2.34 - 2.23 (m, 2H), 1.41 (d, *J*=6.8 Hz, 3H).

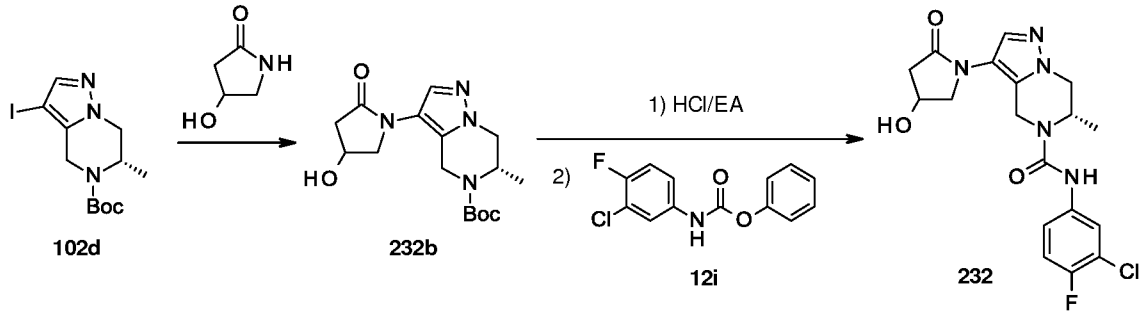
The compound **231c** was prepared in analogy to compound **147c** by using 3-chloro-4,5-difluoro-aniline instead of 3-(1,1-difluoroethyl)aniline (compound **147b**).

Example 232:

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-hydroxy-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:

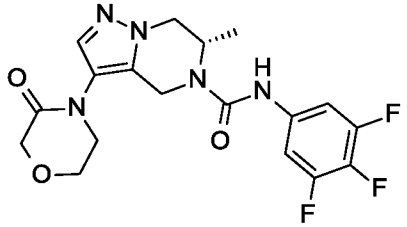


Preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-hydroxy-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 232):

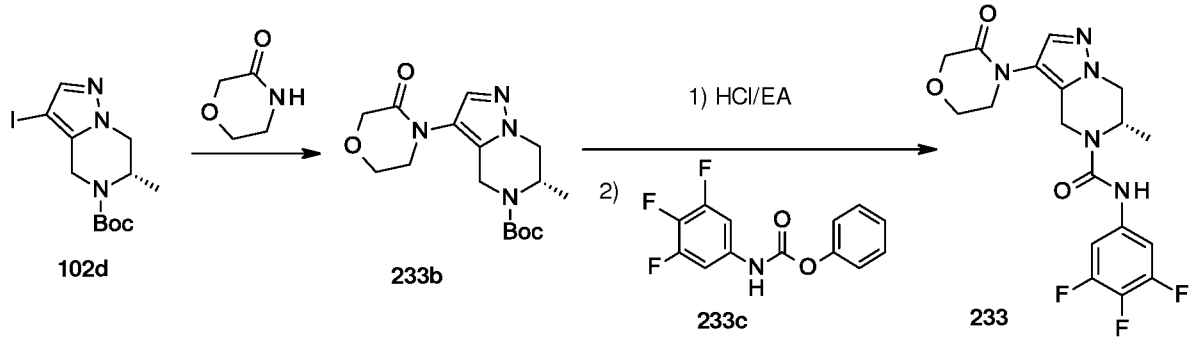
The title compound was prepared in analogy to Example **223** by using 4-hydroxypyrrolidin-2-one instead of pyrrolidin-2-one, and phenyl N-(3-chloro-4-fluoro-phenyl)carbamate (compound **12i**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). Example **232** was obtained as a solid (9.5 mg). LCMS ($M+H^+$): 408. ^1H NMR (400MHz, chloroform-d) δ ppm 7.66 - 7.60 (m, 1H), 7.50 (s, 1H), 7.43 (d, *J*=12.8 Hz, 1H), 7.34 - 7.29 (m, 1H), 7.05 (dt, *J*=5.3, 8.8 Hz, 1H), 5.18 (d, *J*=16.8 Hz, 0.5H), 5.10 (t, *J*=6.8 Hz, 1H), 5.01 (d, *J*=16.6 Hz, 0.5H), 4.77 - 4.69 (m, 1H), 4.48 (d, *J*=16.6 Hz, 0.5H), 4.38 (d, *J*=16.8 Hz, 0.5H), 4.30 (dd, *J*=5.3, 12.8 Hz, 1H), 4.22 - 4.15 (m, 0.5H), 4.10 - 4.03 (m, 1.5H), 3.82 - 3.76 (m, 0.5H), 3.71 - 3.64 (m, 0.5H), 2.97 - 2.88 (m, 1H), 2.63 - 2.53 (m, 1H), 1.36 (dd, *J*=1.5, 7.0 Hz, 3H).

Example 233:

(6S)-6-methyl-3-(3-oxomorpholin-4-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



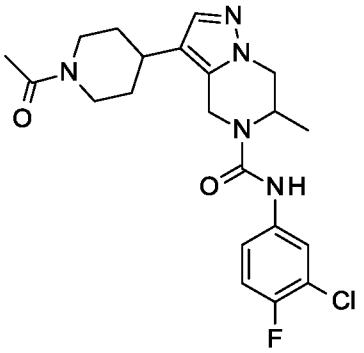
Preparation of (6S)-6-methyl-3-(3-oxomorpholin-4-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 233):

The title compound was prepared in analogy to Example **223** by using morpholin-3-one instead of pyrrolidin-2-one, phenyl N-(3,4,5-trifluorophenyl)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). Example **233** was obtained as a solid (613 mg). LCMS ($M+H^+$): 410. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.07 (s, 1H), 7.63 (s, 1H), 7.47 - 7.39 (m, 2H), 4.91 - 4.82 (m, 2H), 4.31 - 4.11 (m, 5H), 3.97 (t, *J*=5.0 Hz, 2H), 3.79 - 3.65 (m, 2H), 1.13 (d, *J*=6.8 Hz, 3H).

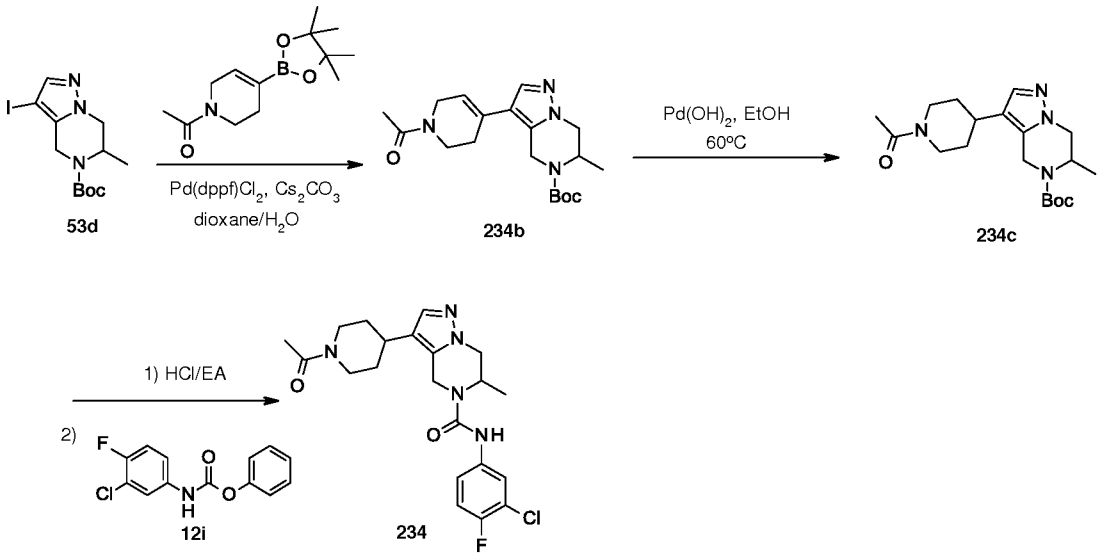
The compound **233c** was prepared in analogy to compound **147c** by using 3,4,5-trifluoroaniline instead of 3-(1,1-difluoroethyl)aniline (compound **147b**).

Example 234:

3-(1-acetyl-4-piperidyl)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:

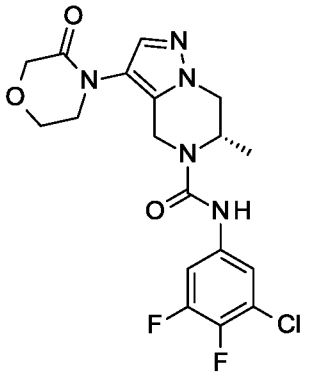


Preparation of 3-(1-acetyl-4-piperidyl)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 234):

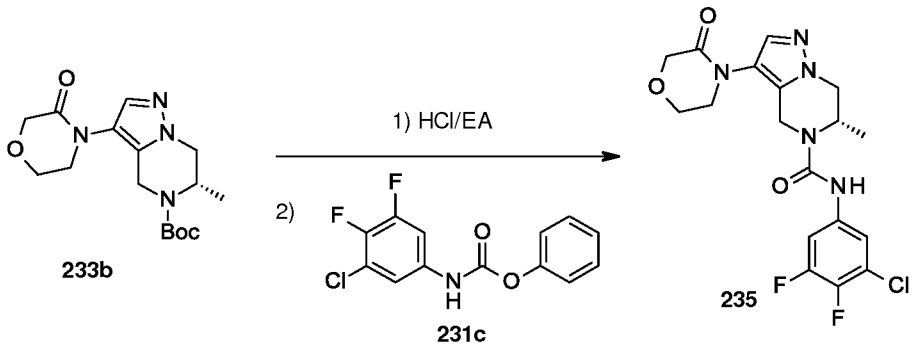
The title compound was prepared in analogy to Example **96** by using 1-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,6-dihydro-2H-pyridin-1-yl]ethanone instead of cyclopenten-1-ylboronic acid. Example **234** was obtained as a solid (22.3 mg). LCMS ($M+H^+$): 434. ^{1}H NMR (400MHz, chloroform-d) δ ppm 7.57 - 7.53 (m, 1H), 7.39 (s, 1H), 7.28 - 7.23 (m, 1H), 7.11 (t, *J*=8.8 Hz, 1H), 6.68 (d, *J*=15.1 Hz, 1H), 4.93 - 4.83 (m, 2H), 4.75 (d, *J*=11.5 Hz, 1H), 4.49 (dd, *J*=3.6, 15.4 Hz, 1H), 4.36 - 4.29 (m, 1H), 4.22 - 4.16 (m, 1H), 3.94 (d, *J*=13.8 Hz, 1H), 3.22 - 3.14 (m, 1H), 2.74 - 2.61 (m, 2H), 2.15 (s, 3H), 1.97 - 1.85 (m, 2H), 1.70 - 1.63 (m, 1H), 1.58 - 1.51 (m, 1H), 1.26 (dd, *J*=2.8, 6.8 Hz, 3H).

Example 235:

(6S)-N-(3-chloro-4,5-difluoro-phenyl)-6-methyl-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:

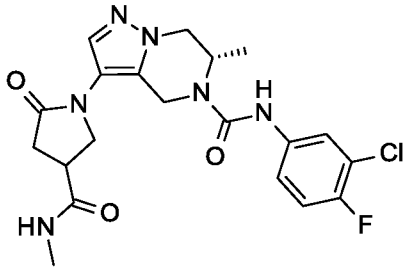


Preparation of (6S)-N-(3-chloro-4,5-difluoro-phenyl)-6-methyl-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 235):

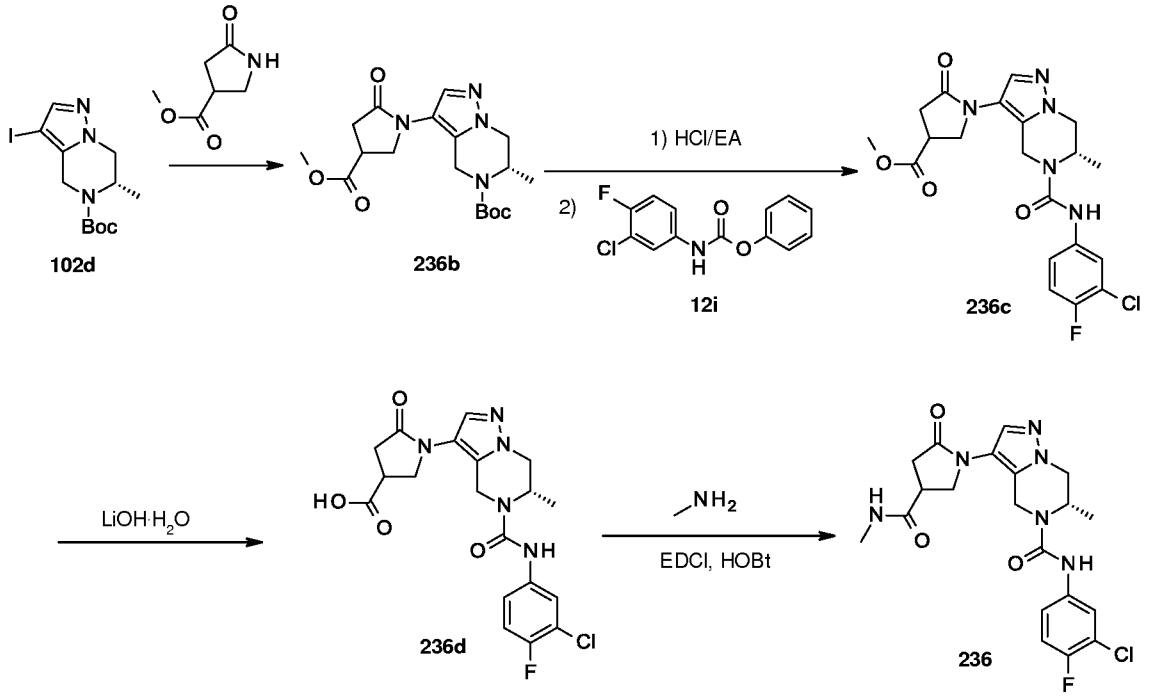
The title compound was prepared in analogy to the preparation of Example **223** by using phenyl N-(3-chloro-4,5-difluoro-phenyl)carbamate (compound **231c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**), and tert-butyl (6S)-6-methyl-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **233b**) instead of tert-butyl (6S)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **223b**). Example **235** was obtained as a solid (37.8 mg). LCMS ($M+H^+$): 426. ^{1}H NMR (400MHz, chloroform-d) δ ppm 7.76 (s, 1H), 7.52 (s, 1H), 7.45 - 7.32 (m, 2H), 5.08 (t, *J*=6.7 Hz, 1H), 4.88 (d, *J*=16.8 Hz, 1H), 4.40 (s, 2H), 4.34 - 4.27 (m, 2H), 4.16 - 4.01 (m, 3H), 4.01 - 3.92 (m, 1H), 3.78 - 3.69 (m, 1H), 1.41 (d, *J*=7.0 Hz, 3H).

Example 236:

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-[4-(methylcarbamoyl)-2-oxo-pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of methyl 1-[(6S)-5-[(3-chloro-4-fluoro-phenyl)carbamoyl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-5-oxo-pyrrolidine-3-carboxylate (compound 236c)

Compound **236c** was prepared in analogy to Example **223** by using methyl 5-oxopyrrolidine-3-carboxylate instead of pyrrolidin-2-one and phenyl N-(3-chloro-4-fluoro-phenyl)carbamate (compound **12i**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). Compound **236c** was obtained as a solid (132 mg). LCMS ($M+H^+$): 450.

Preparation of 1-[(6S)-5-[(3-chloro-4-fluoro-phenyl)carbamoyl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-5-oxo-pyrrolidine-3-carboxylic acid (compound 236d)

To a solution of methyl 1-[(6S)-5-[(3-chloro-4-fluoro-phenyl)carbamoyl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-5-oxo-pyrrolidine-3-carboxylate (compound **236c**, 120 mg, 0.27 mmol) in tetrahydrofuran (0.6 mL) was added lithium hydroxide monohydrate (56 mg, 1.33 mmol) in water (0.6 mL). The reaction mixture was stirred at room temperature for 3 hours.

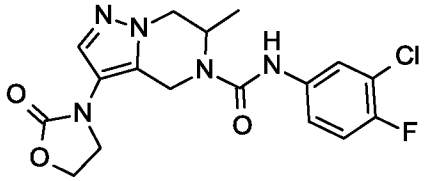
Then the reaction mixture was neutralized with 1N solution of hydrogen chloride in ethyl acetate, diluted with tetrahydrofuran and dried. The organic phase was separated and concentrated. The residue was purified by prep-HPLC to give compound **236d** (51 mg). LCMS ($M+H^+$): 436.

Preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-[4-(methylcarbamoyl)-2-oxo-pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 236):

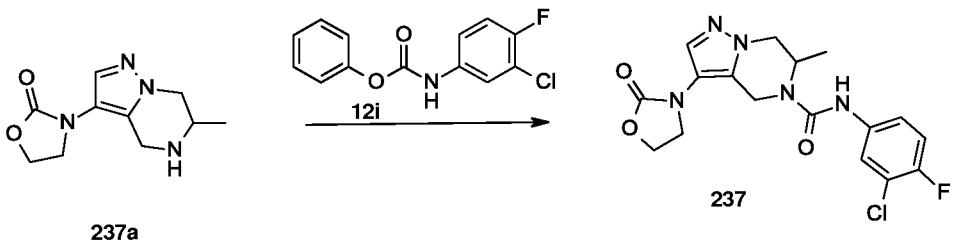
To a solution of compound 1-[(6S)-5-[(3-chloro-4-fluoro-phenyl)carbamoyl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-5-oxo-pyrrolidine-3-carboxylic acid (**236d**, 20 mg, 45.9 μmol) in dichloromethane (3.0 mL) were added methanamine hydrochloride (9.3 mg, 138 μmol), 1-ethyl-3- 3-dimethylaminopropyl carbodiimide hydrochloride (11.4 mg, 59.7 μmol), 1-hydroxybenzotriazole (1.9 mg, 13.8 μmol) and diisopropylethylamine (29.7 mg, 39.3 μL). The reaction mixture was stirred at room temperature for 2 hours. The reaction mixture was washed with water, extracted with dichloromathane twice. The organic phases were combined and dried over Na_2SO_4, filtrated and concentrated. The residue was purified by silica gel column to afford Example **236** (14.3 mg). LCMS ($M+H^+$): 449. ^{1}H NMR (400MHz, chloroform-d) δ ppm 7.66 - 7.54 (m, 2H), 7.45 (d, *J*=5.3 Hz, 1H), 7.36 - 7.29 (m, 1H), 7.04 (t, *J*=8.8 Hz, 1H), 5.78 (br. s., 1H), 5.16 - 5.03 (m, 2H), 4.43 (dd, *J*=5.1, 16.7 Hz, 1H), 4.32 - 4.22 (m, 1H), 4.11 - 3.89 (m, 3H), 3.27 - 3.18 (m, 1H), 2.94 - 2.76 (m, 5H), 1.35 (dd, *J*=4.0, 7.0 Hz, 3H).

Example 237:

N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(2-oxooxazolidin-3-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



237a

237

Preparation of 3-(6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)oxazolidin-2-one (compound 237a)

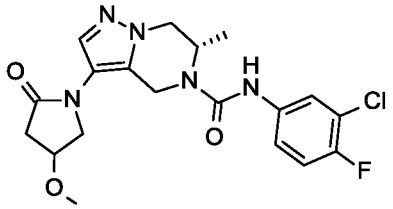
Compound **237a** was prepared in analogy to 4,4-dimethyl-1-(6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)pyrrolidin-2-one (compound **212b)** by using oxazolidin-2-one instead of 4,4-dimethylpyrrolidin-2-one.

Preparation of N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(2-oxooxazolidin-3-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 237):

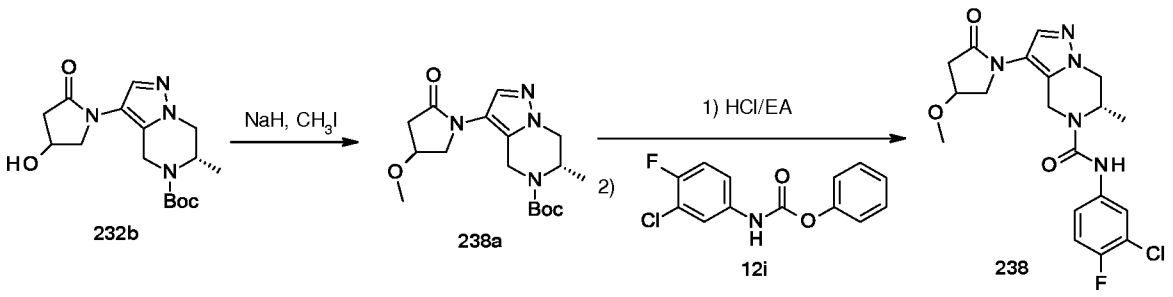
The title compound was prepared in analogy to the preparation of Example **140** by using phenyl N-(3-chloro-4-fluoro-phenyl)carbamate (compound **12i**) instead of phenyl N-(6-chloro-5-fluoro-2-pyridyl)carbamate (compound **140d**) and 3-(6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)oxazolidin-2-one (compound **237a**) instead of 3-(4-fluorophenyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **11b**). Example **237** was obtained as a white solid. LCMS ($M+H^+$): 394. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 8.95 (s, 1H), 7.74 (dd, *J*=2.4, 6.9 Hz, 1H), 7.62 (s, 1H), 7.44 - 7.42 (m, 1H), 7.35 - 7.27 (m, 1H), 5.05 (d, *J*=16.8 Hz, 1H), 4.89 (t, *J*=16.6 Hz, 1H), 4.47 - 4.36 (m, 3H), 4.13 - 4.07 (m, 2H), 4.01 - 3.92 (m, 2H), 1.14 (d, *J*=6.8 Hz, 3H).

Example 238:

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-methoxy-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of tert-butyl (6S)-3-(4-methoxy-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 238a):

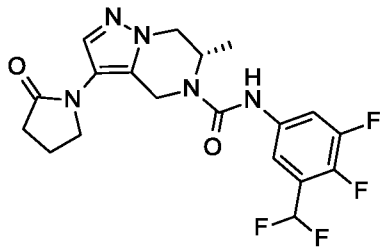
Compound **238a** was prepared in analogy to compound **210b** by using compound **232b** instead of tert-butyl 3-(hydroxymethyl)pyrrolidine-1-carboxylate (compound **210a**).

Preparation of ((6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-methoxy-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 238):

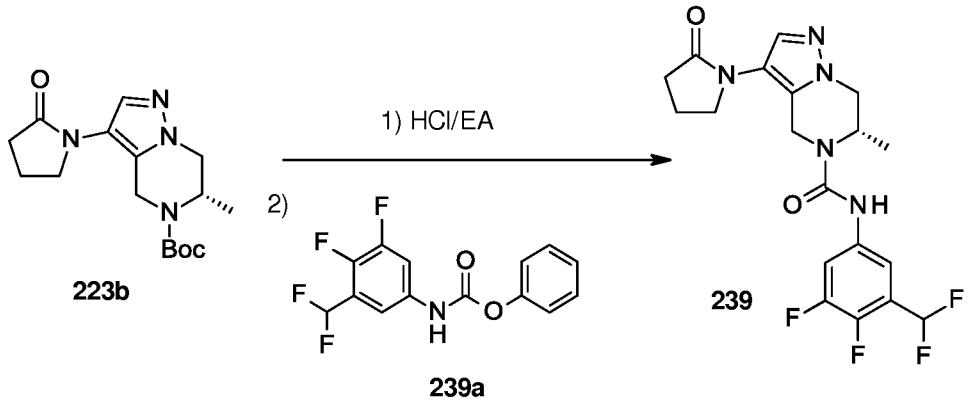
The title compound was prepared in analogy to the preparation of Example **223** by using compound **238a** and compound **12i** instead of compounds **223b** and **218c**, respectively. Example **238** was obtained as a solid. LCMS ($M+H^+$): 422. ^1H NMR (400MHz, DMSO-d_6) δ ppm 8.95 (d, *J*=5.0 Hz, 1H), 7.73 (dd, *J*=2.4, 6.9 Hz, 1H), 7.62 (d, *J*=6.0 Hz, 1H), 7.45 - 7.38 (m, 1H), 7.36 - 7.28 (m, 1H), 4.98 (t, *J*=16.6 Hz, 1H), 4.90 - 4.82 (m, 1H), 4.47 - 4.30 (m, 1H), 4.24 - 4.17 (m, 1H), 4.17 - 4.08 (m, 2H), 4.07 - 3.95 (m, 1H), 3.75 - 3.64 (m, 1H), 3.29 (d, *J*=3.0 Hz, 3H), 2.81 - 2.70 (m, 1H), 2.35 (d, *J*=10.8 Hz, 1H), 1.26 - 1.08 (m, 3H)

Example 239:

(6S)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of phenyl N-[3-(difluoromethyl)-4,5-difluoro-phenyl]carbamate (compound 239a):

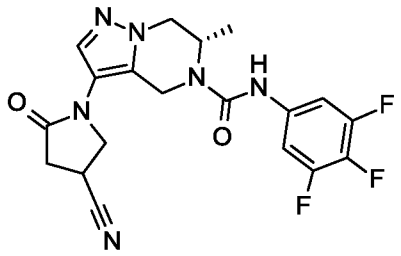
Compound **239a** was prepared in analogy to compound **147c** by using 5-bromo-1-(difluoromethyl)-2,3-difluoro-benzene (catalog number: ABF12819, Shanghai AQBioPharma Co. Ltd) instead of 1-bromo-3-(1,1-difluoroethyl)benzene.

Preparation of (6S)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 239):

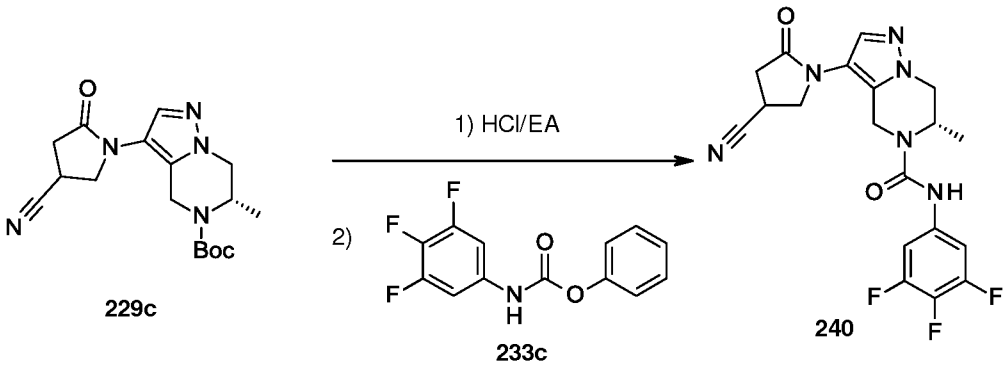
The title compound was prepared in analogy to Example **223** by using phenyl N-[3-(difluoromethyl)-4,5-difluoro-phenyl]carbamate (compound **239a**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl] (compound **218c**). Example **239** was obtained as a solid (50 mg). LCMS ($M+H^+$): 426. ^1H NMR (400MHz, MeOD) δ ppm 7.74 - 7.66 (m, 1H), 7.63 (s, 1H), 7.49 - 7.43 (m, 1H), 7.01 (t, *J*=48 Hz, 2H), 5.05 (d, *J*=16.8 Hz, 1H), 5.01 - 4.94 (m, 1H), 4.52 (d, *J*=17.1 Hz, 1H), 4.31 (dd, *J*=4.5, 12.8 Hz, 1H), 4.17 (d, *J*=13.8 Hz, 1H), 3.93 - 3.81 (m, 2H), 2.62 - 2.52 (m, 2H), 2.33 - 2.17 (m, 2H), 1.28 (d, *J*=7.0 Hz, 3H).

Example 240:

(6S)-3-(4-cyano-2-oxo-pyrrolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of (6S)-3-(4-cyano-2-oxo-pyrrolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 240):

The title compound was prepared in analogy to Example **220** by using phenyl N-(3,4,5-trifluorophenyl)carbamate (compound **233c**) instead of phenyl N-(3-chloro-4-fluoro-phenyl)carbamate (compound **12i**) and tert-butyl (6S)-3-(4-cyano-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **229c**) instead of tert-

butyl 3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **220b**). Example **240** was obtained as a solid (40 mg). LCMS ($M+H^+$): 419. ^1H NMR (400MHz, MeOD) δ ppm 7.65 (d, *J*=1.8 Hz, 1H), 7.35 - 7.25 (m, 2H), 5.04 (d, *J*=17.1 Hz, 1H), 5.00 - 4.93 (m, 1H), 4.50 (d, *J*=17.3 Hz, 1H), 4.35 - 4.26 (m, 1H), 4.21 - 4.02 (m, 3H), 3.83 - 3.73 (m, 1H), 3.05 - 2.94 (m, 1H), 2.92 - 2.81 (m, 1H), 1.29-1.26 (m, 3H).

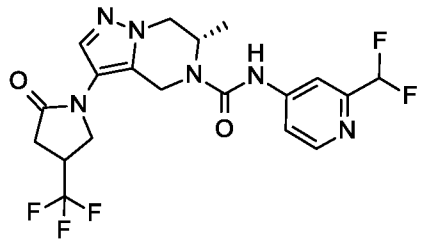
Example **240** was subjected to chiral separation to give Example **240-1** and Example **240-2** with the names of these two compounds: **(6S)-3-[(4R)-4-cyano-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide** and **(6S)-3-[(4S)-4-cyano-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide**. (Preparative SFC conditions: Column: AD-H, 250×20 mm I.D.; Mobile phase: A for CO_2, B for MeOH; Eluent: B 30%; Flow rate: 65mL /min; Back pressure: 100bar; column temperature: 35 °C).

Example **240-1** (Retention time, 1.95 min). LCMS ($M+H^+$): 419. ^1H NMR (400MHz, MeOD) δ ppm 7.65 (s, 1H), 7.28 (dd, *J*=6.5, 10.3 Hz, 2H), 5.04 (d, *J*=17.1 Hz, 1H), 4.99 - 4.92 (m, 1H), 4.50 (d, *J*=17.1 Hz, 1H), 4.31 (dd, *J*=4.3, 12.5 Hz, 1H), 4.22 - 4.11 (m, 2H), 4.05 (dd, *J*=6.3, 9.8 Hz, 1H), 3.86 - 3.71 (m, 1H), 3.00 (dd, *J*=9.3, 17.1 Hz, 1H), 2.86 (dd, *J*=9.3, 17.1 Hz, 1H), 1.27 (d, *J*=6.8 Hz, 3H).

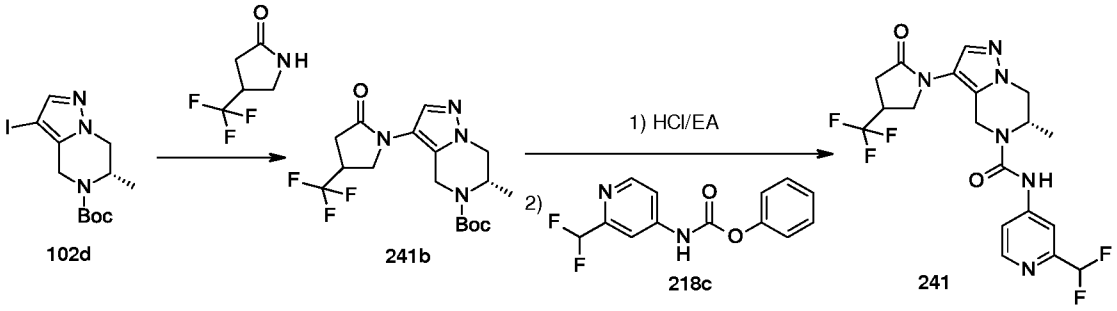
Example **240-2** (Retention time, 2.72 min). LCMS ($M+H^+$): 419. ^1H NMR (400MHz, MeOD) δ ppm 7.65 (s, 1H), 7.28 (dd, *J*=6.3, 10.3 Hz, 2H), 5.04 (d, *J*=16.8 Hz, 1H), 4.98 - 4.93 (m, 1H), 4.50 (d, *J*=16.8 Hz, 1H), 4.30 (dd, *J*=4.5, 12.8 Hz, 1H), 4.21 - 4.04 (m, 3H), 3.85 - 3.71 (m, 1H), 3.00 (dd, *J*=9.3, 17.1 Hz, 1H), 2.88 (dd, *J*=9.3, 17.1 Hz, 1H), 1.28 (d, *J*=7.0 Hz, 3H).

Example 241:

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-6-methyl-3-[2-oxo-4-(trifluoromethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:

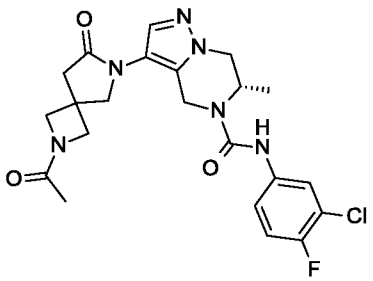


Preparation of (6S)-N-[2-(difluoromethyl)-4-pyridyl]-6-methyl-3-[2-oxo-4-(trifluoromethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 241):

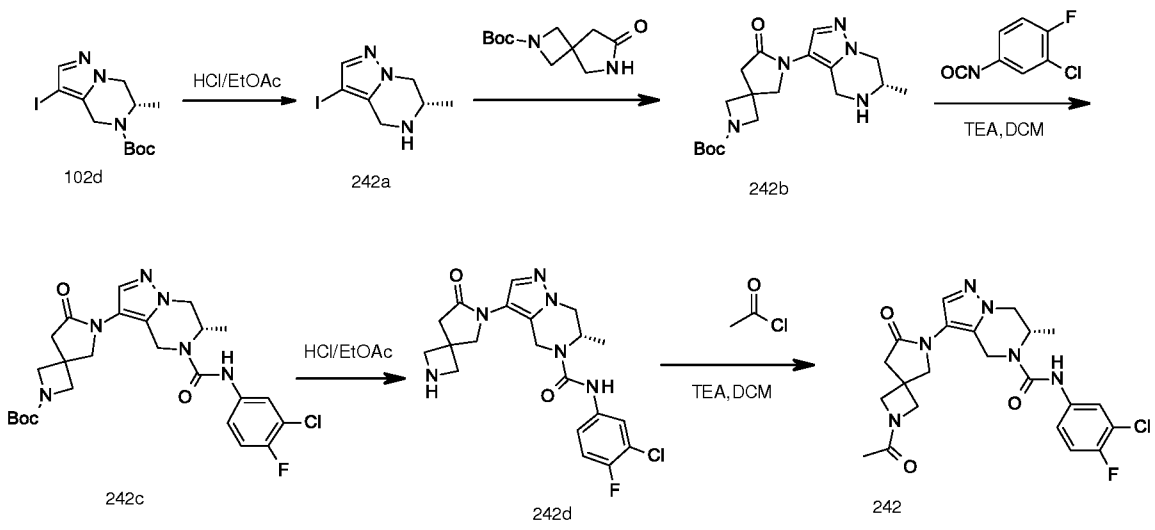
The title compound was prepared in analogy to Example **220** by using 4-(trifluoromethyl)pyrrolidin-2-one instead of morpholin-3-one, phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**) instead of phenyl N-(3-chloro-4-fluoro-phenyl)carbamate (compound **12i**) and tert-butyl (6S)-3-iodo-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **102d**) instead of tert-butyl 3-iodo-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **1e**). Example **241** was obtained as a solid (18 mg). LCMS ($M+H^+$): 459. ^{1}H NMR (400MHz, MeOD) δ ppm 8.42 (d, *J*=5.8 Hz, 1H), 7.86 (s, 1H), 7.71 - 7.62 (m, 2H), 6.67 (t, *J*=48.0 Hz, 1H), 5.11 (d, *J*=12.3 Hz, 0.5H), 5.07 (d, *J*=12.0 Hz, 0.5H), 5.03 - 4.95 (m, 1H), 4.55 (d, *J*=9.8 Hz, 0.5H), 4.51 (d, *J*=9.8 Hz, 0.5H), 4.33 (td, *J*=3.6, 12.8 Hz, 1H), 4.22 - 4.07 (m, 2H), 3.98-3.91 (m, 1H), 3.59 - 3.45 (m, 1H), 2.98 - 2.87 (m, 1H), 2.76 - 2.65 (m, 1H), 1.30 (dd, *J*=3.5, 6.8 Hz, 3H)

Example 242:

(6S)-3-(2-acetyl-7-oxo-2,6-diazaspiro[3.4]octan-6-yl)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: preparation of (6S)-3-iodo-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound 242a)

To a mixture of tert-butyl (6S)-3-iodo-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **102d**, 2.0 g, 5.5 mmol) was added HCl/EtOAc (50.0 mL) and the reaction mixture was stirred at room temperature for 1 hour. The solvent was removed in *vacuo*, the residue was basified by K_2CO_3 in DCM (100.0 mL). The solid was filtered off and organic layer was evaporated to give compound **242a** (1.3 g). LCMS ($M+H^+$): 263.

Step 2: preparation of tert-butyl 6-[(6S)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl]-7-oxo-2,6-diazaspiro[3.4]octane-2-carboxylate (compound 242b)

To a solution of tert-butyl 6-oxo-2,7-diazaspiro[3.4]octane-2-carboxylate (271.5 mg, 1.2 mmol) in dioxane (15 mL) was added (6S)-3-iodo-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine(compound **242a**, 263.0 mg, 1.0 mmol), (1R,2R)-N1,N2-dimethylcyclohexane-1,2-diamine (14.2 mg, 0.1 mmol), K_3PO_4 (637.0 mg, 3.0 mmol) and CuI (19.0 mg, 0.1 mmol) under N_2, and the reaction mixture was stirred at 120 °C for 12 hours, then filtered and concentrated under the reduce pressure, the residue was purified by silica gel column chromatography (DCM/MeOH=50/1 to 20/1) to give compound **242b** (200 mg) as white oil. LCMS ($M+H^+$): 362.

Step 3: preparation of tert-butyl 6-[(6S)-5-[(3-chloro-4-fluoro-phenyl)carbamoyl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-7-oxo-2,6-diazaspiro[3.4]octane-2-carboxylate (compound 242c)

To a solution of tert-butyl 6-[(6S)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl]-7-oxo-2,6-diazaspiro[3.4]octane-2-carboxylate (compound **242b**, 94.9 mg, 0.55 mmol) and Et_3N (111.7 mg, 1.106 mmol) in DCM (5 mL) was added 2-chloro-1-fluoro-4-isocyanato-

benzene (200.0 mg, 0.55 mmol) at 20 °C, and then the reaction mixture was stirred at 20 ℃ for 1 hour. Then the reaction mixture was diluted with water, extracted with EtOAc (50 mL). The organic layer was dried over Na_2SO_4 and evaporated to dryness to give compound **242c** (280.0 mg) as white solid. LCMS ($M+H^+$): 533.

Step 4: preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(7-oxo-2,6-diazaspiro[3.4]octan-6-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (compound 242d)

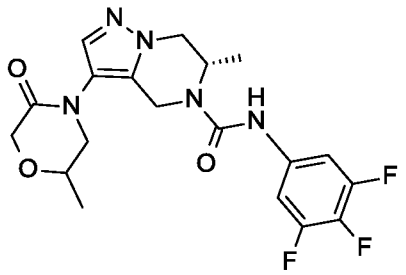
To a mixture of tert-butyl 6-[(6S)-5-[(3-chloro-4-fluoro-phenyl)carbamoyl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-7-oxo-2,6-diazaspiro[3.4]octane-2-carboxylate(compound **242c**, 100.0 mg, 0.188 mmol) was added HCl/EtOAc (10 mL) and the reaction mixture was stirred for 1 hour. Then the solvent was removed in *vacuo* to give compound **242d** (88 mg). LCMS ($M+H^+$): 433.

Step 5: preparation of (6S)-3-(2-acetyl-7-oxo-2,6-diazaspiro[3.4]octan-6-yl)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 242)

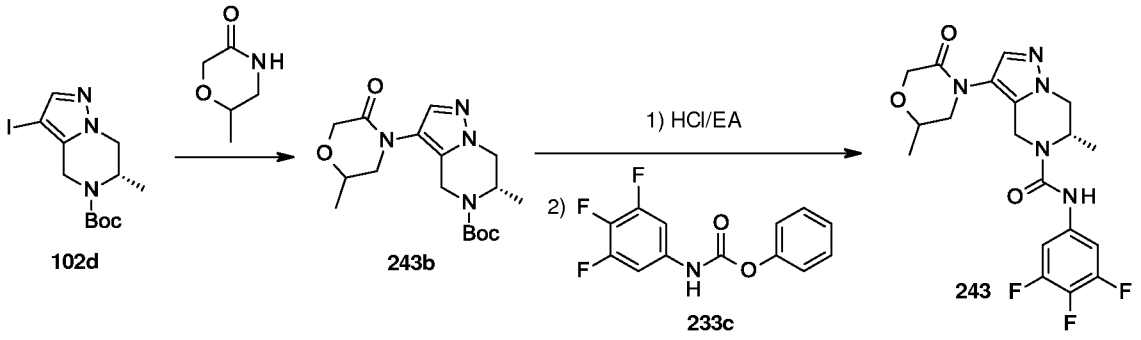
To a solution of (6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(7-oxo-2,6-diazaspiro[3.4]octan-6-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (compound **242d**, 88.0 mg, 0.187 mmol) in DCM (10.0 mL) was added Et_3N (37.8 mg, 0.374 mmol) and acetyl chloride (30.5 mg, 0.281 mmol). The reaction mixture was stirred at room temperature for 1 hour. A few drops of water was added, the solvent was removed in *vacuo*, the residue was purified by prep-HPLC to give Example **242** (20 mg) as white solid. LCMS ($M+H^+$): 475. ^1H NMR (400MHz, DMSO-d_6) δ ppm 8.99 (s, 1H), 7.74 (dd, *J*=2.3, 6.8 Hz, 1H), 7.61 (s, 1H), 7.47 - 7.39 (m, 1H), 7.37 - 7.27 (m, 1H), 5.03 - 4.94 (m, 1H), 4.90 - 4.81 (m, 1H), 4.37 (dd, *J*=2.9, 17.2 Hz, 1H), 4.25 - 4.07 (m, 4H), 4.04 - 3.85 (m, 4H), 2.80 - 2.72 (m, 2H), 1.77 (s, 3H), 1.14 (d, *J*=6.3 Hz, 3H).

Example 243:

(6S)-6-methyl-3-(2-methyl-5-oxo-morpholin-4-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:

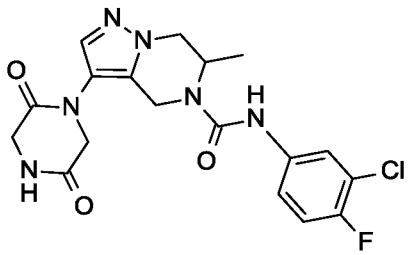


Preparation of (6S)-6-methyl-3-(2-methyl-5-oxo-morpholin-4-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 243):

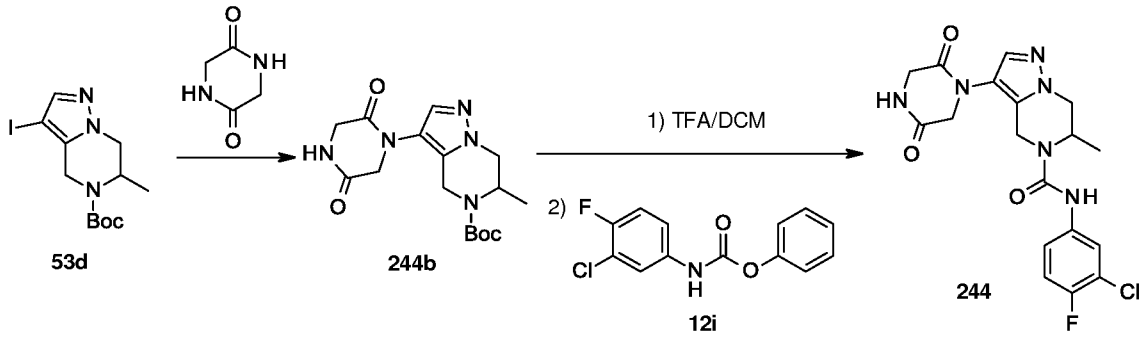
The title compound was prepared in analogy to Example **223** by using 6-methylmorpholin-3-one instead of pyrrolidin-2-one, and phenyl N-(3,4,5-trifluorophenyl)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 243** was obtained as a solid (63 mg). LCMS ($M+H^+$): 424. ^1H NMR (400MHz, chloroform-d) δ ppm 7.96 - 7.75 (m, 1H), 7.51 (s, 1H), 7.28 - 7.18 (m, 2H), 5.15 - 5.03 (m, 1H), 4.95 - 4.78 (m, 1H), 4.51 - 4.42 (m, 1H), 4.40 - 4.22 (m, 3H), 4.17 - 3.97 (m, 2H), 3.85 - 3.68 (m, 1H), 3.65 - 3.50 (m, 1H), 1.46 - 1.36 (m, 6H).

Example 244:

N-(3-chloro-4-fluoro-phenyl)-3-(2,5-dioxopiperazin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: **preparation of tert-butyl 3-(2,5-dioxopiperazin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 244b):**

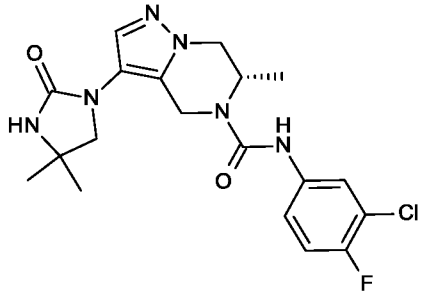
The reaction mixture of piperazine-2,5-dione (1.41 g, 12.4 mmol), tert-butyl 3-iodo-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **53d**, 300 mg, 826 μmol), K_3PO_4 (351 mg, 1.65 mmol), CuI (31.5 mg, 165 μmol) and (1R,2R)-N1,N2-dimethylcyclohexane-1,2-diamine (23.5 mg, 165 μmol) in DMSO (15 mL) was flushed with nitrogen and sealed. The reaction mixture was heated to 105 °C in microwave for 1 hour. The reaction mixture was cooled down. After diluted with ethyl acetate, the reaction mixture was washed with ice-water, extracted by ethyl acetate three times. Then the combined organic layer was dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by column to give compound **244b** (144 mg). LCMS ($M+H^+$): 350.

Step 2: preparation of N-(3-chloro-4-fluoro-phenyl)-3-(2,5-dioxopiperazin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 244):

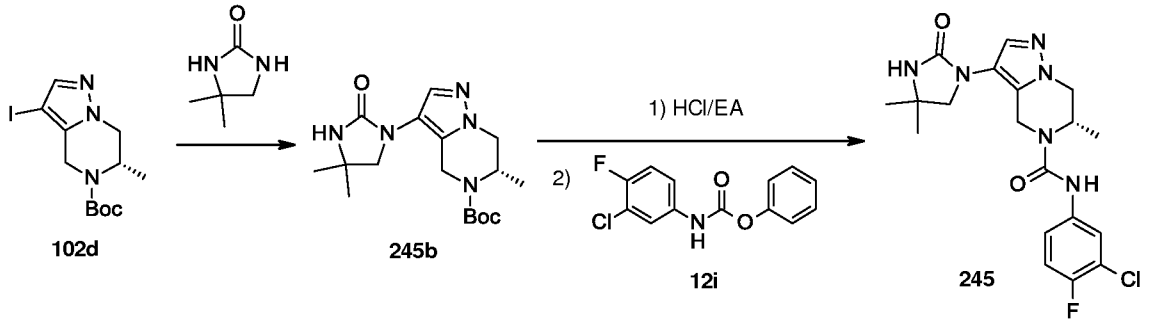
A mixture of tert-butyl 3-(2,5-dioxopiperazin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **244b**, 100 mg, 286 μmol) trifluoroacetic acid (2 mL, 26 mmol,) and DCM (1 mL) was stirred at room temperature for 1 hour. The reaction mixture was concentrated, the residue was dissolved in DMF (3 mL), then DIPEA (754 mg, 1 mL, 5.83 mmol) and phenyl (3-chloro-4-fluorophenyl)carbamate (compound **12i**, 114 mg, 429 μmol) were added. The reaction mixture was stirred at 40 °C for 3 hours. The reaction mixture was purified by prep-HPLC to give **Example 244** (16 mg). LCMS ($M+H^+$): 421. ^1H NMR (400MHz, chloroform-d) δ ppm 7.63 - 7.55 (m, 1H), 7.52 (s, 1H), 7.31 - 7.29 (m, 1H), 7.19 (s, 1H), 7.08 (s, 1H), 6.35 - 6.26 (m, 1H), 5.12 - 5.03 (m, 1H), 4.86 (d, *J*=16.6 Hz, 1H), 4.53 - 4.45 (m, 1H), 4.35 (dd, *J*=5.6, 16.9 Hz, 3H), 4.24 (s, 2H), 4.11 (d, *J*=13.8 Hz, 1H), 1.36 (d, *J*=7.0 Hz, 3H).

Example 245:

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4,4-dimethyl-2-oxo-imidazolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:

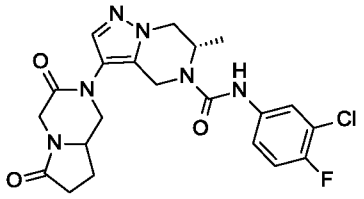


Preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-hydroxy-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 232):

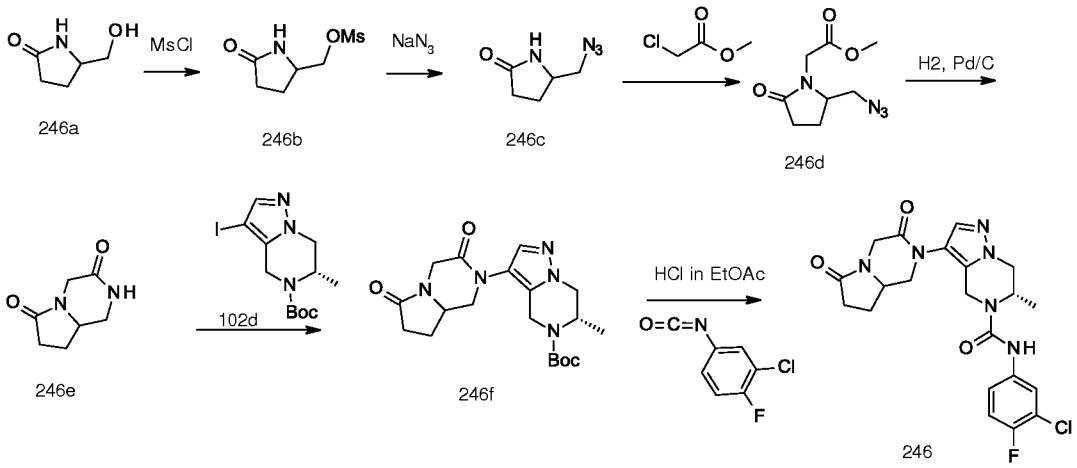
The title compound was prepared in analogy to **Example 223** by using 4,4-dimethylimidazolidin-2-one instead of pyrrolidin-2-one, and phenyl N-(3-chloro-4-fluoro-phenyl)carbamate (compound **12i**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 245** was obtained as a solid (8.6 mg). LCMS ($M+H^+$): 421. ^1H NMR (400MHz, chloroform-d) δ ppm 7.75 (s, 1H), 7.65 (dd, *J*=2.8, 6.5 Hz, 1H), 7.39 - 7.30 (m, 2H), 7.05 (t, *J*=8.9 Hz, 1H), 5.18 (d, *J*=16.8 Hz, 1H), 5.09 (s, 1H), 4.54 (s, 1H), 4.41 (d, *J*=16.8 Hz, 1H), 4.28 (dd, *J*=5.3, 12.8 Hz, 1H), 4.03 (d, *J*=2.0 Hz, 1H), 3.73 (d, *J*=8.5 Hz, 1H), 3.56 (d, *J*=8.5 Hz, 1H), 1.47 (s, 3H), 1.45 (s, 3H), 1.39 (d, *J*=7.0 Hz, 3H).

Example 246:

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(3,6-dioxo-4,7,8,8a-tetrahydro-1H-pyrrolo[1,2-a]pyrazin-2-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: preparation of (5-oxopyrrolidin-2-yl)methyl methanesulfonate (compound 246b)

To a mixture of compound **246a** (2.0 g, 17.4 mmol) and TEA (5.3 g, 52 mmol) in DCM (20 mL) was added MsCl (5.97 g, 52 mmol) at 0 °C. The resulting mixture was stirred at room temperature for 3 hours, and then concentrated and purified by silica gel chromatography to afford compound **246b** as a white solid (3.2 g).

Step 2: preparation of 5-(azidomethyl)pyrrolidin-2-one (compound 246c)

To a solution of (5-oxopyrrolidin-2-yl)methyl methanesulfonate (compound **246b**, 1.0 g, 5.2 mmol) in DMF (20.0 mL) was added NaN_3 (2.51 g, 38.5 mmol) and K_2CO_3 (5.32 g, 38.5 mmol). The reaction mixture was heated to 80 °C for 16 hours. The reaction mixture was filtered, and the filtrate was concentrated and purified by chromatography (PE/EtOAc=1/1 to pure EtOAc) to give compound **246c** as yellow oil (0.3 g).

Step 3: preparation of methyl 2-[2-(azidomethyl)-5-oxo-pyrrolidin-1-yl]acetate (compound 246d)

To a solution of 5-(azidomethyl)pyrrolidin-2-one (compound **246c**, 100.0 mg, 0.71 mmol) in THF (5.0 mL) was added NaH (42.8 mg, 1.07 mmol) at 0 °C, the reaction mixture was warmed to room temperature and stirred for 1 hour. Then the reaction mixture was cooled to 0 °C and methyl 2-chloroacetate (116.2 mg, 1.07 mmol) was added and the reaction mixture was stirred at room temperature for 16 hours. Then the reaction mixture was concentrated and the

residue was purified by prep-TLC (EtOAc) to give compound **246d** (80.0 mg) as colorless oil. LCMS ($M+H^+$): 213.

Step 4: preparation of 1,2,4,7,8,8a-hexahydropyrrolo[1,2-a]pyrazine-3,6-dione (compound 246e)

To a solution of methyl 2-[2-(azidomethyl)-5-oxo-pyrrolidin-1-yl]acetate (compound **246d**, 80.0 mg, 0.38 mmol) in MeOH (5.0 mL) was added Pd/C (10.0 mg) under N_2. The reaction mixture was stirred at room temperature under H_2 (50 psi) for 16 hours. The reaction mixture was filtered and the filtrate was concentrated to give compound **246e** as a red oil (50.0 mg). LCMS ($M+H^+$): 155.

Step 5: preparation of tert-butyl (6S)-3-(3,6-dioxo-4,7,8,8a-tetrahydro-1H-pyrrolo[1,2-a]pyrazin-2-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 246f)

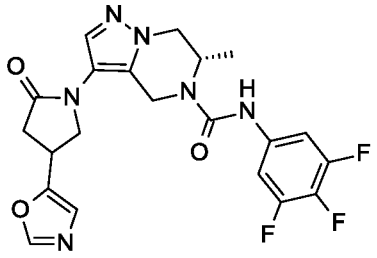
The reaction mixture of tert-butyl (6S)-3-iodo-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **102d**, 117.8 mg, 0.32 mmol), 1,2,4,7,8,8a-hexahydropyrrolo[1,2-a]pyrazine-3,6-dione (compound **246e**, 50.0 mg, 0.32 mmol), (1R,2R)-N1,N2-dimethylcyclohexane-1,2-diamine (4.6 mg, 0.03 mmol), CuI (6.1 mg, 0.03 mmol) and K_3PO_4 (135.9 mg, 0.64 mmol) in dioxane (5.0 mL) was degassed and stirred at 120 °C under N_2 for 16 hours. The reaction mixture was concentrated and purified by silica gel chromatography (DCM/MeOH=20/1) to give compound **246f** as yellow oil (28.0 mg). LCMS ($M+H^+$): 390

Step 6: preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-3-(3,6-dioxo-4,7,8,8a-tetrahydro-1H-pyrrolo[1,2-a]pyrazin-2-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 246)

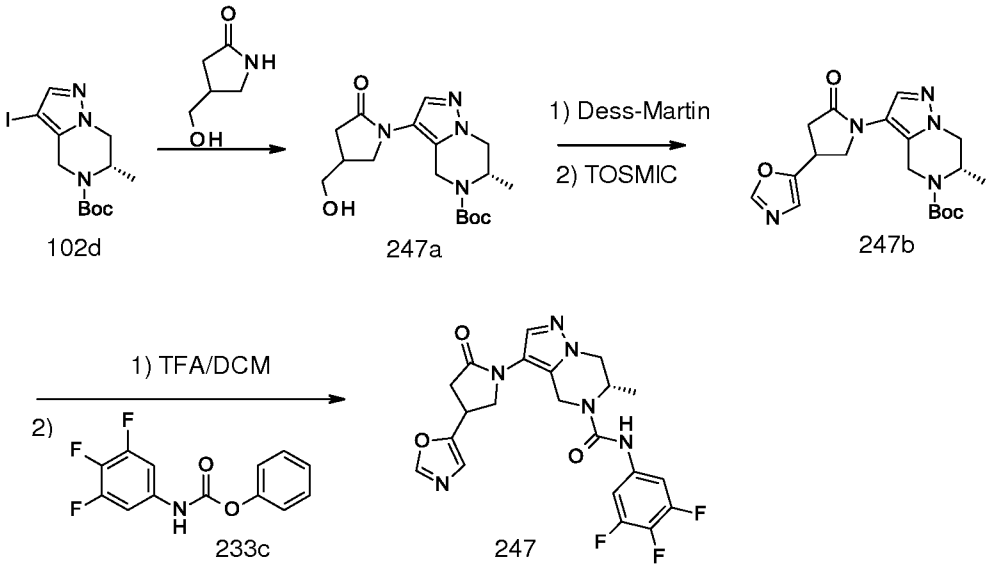
A solution of tert-butyl (6S)-3-(3,6-dioxo-4,7,8,8a-tetrahydro-1H-pyrrolo[1,2-a]pyrazin-2-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **246f**, 100.0 mg, 0.26 mmol) in HCl/EtOAc (5.0 mL) was stirred at room temperature for 2 hours. The reaction mixture was concentrated and the residue was added to a solution of Et_3N (37.3 mg, 0.368 mmol) in DCM (5.0 mL). Then 2-chloro-1-fluoro-4-isocyanato-benzene (21.1 mg, 0.123 mmol) was added and stirred at room temperature for 1 hour. The reaction mixture was concentrated, the residue was purified by prep-HPLC to give Example **246** as white solid (10.0 mg). LCMS ($M+H^+$): 461. ^1H NMR (400MHz, MeOD) δ ppm 7.70-7.55 (m, 2H), 7.33 (dt, *J*=8.9, 3.4 Hz, 1H), 7.24-7.09 (m, 1H), 5.03-4.91 (m, 2H), 4.57-4.10 (m, 5H), 3.93 (d, *J*=18.4 Hz, 1H), 3.88-3.67 (m, 2H), 2.59-2.50 (m, 2H), 2.46-2.32 (m, 1H), 1.92-1.79 (m, 1H), 1.27 (t, *J*=7.3 Hz, 3H).

Example 247:

(6S)-6-methyl-3-(4-oxazol-5-yl-2-oxo-pyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: preparation of (6S)-tert-butyl 3-(4-(hydroxymethyl)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 247a)

To a 20 mL microwave vial was added tert-butyl (6S)-3-iodo-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **102d**, 1 g, 2.75 mmol), 4-(hydroxymethyl)pyrrolidin-2-one (634 mg, 5.51 mmol), copper (I) iodide (105 mg, 0.55 mmol), potassium phosphate (1.17 g, 5.51 mmol), (1R,2R)-N1,N2-dimethylcyclohexane-1,2-diamine (157 mg, 1.1 mmol), and DMSO (15 mL). The vial was sealed and heated in microwave at 105 °C for 1 hour. The reaction mixture was poured into 50 mL of H_2O and extracted with EtOAc (50 mL) twice. The organic layers were combined and then concentrated in *vacuo* to give a residue, which was purified by flash chromatography (silica gel, 0% to 80% EtOAc(contain 10% MeOH) in hexanes) to give compound **247a** (800 mg) as light yellow oil. LCMS ($M+H^+$): 351

Step 2: preparation of (6S)-tert-butyl 6-methyl-3-(4-(oxazol-5-yl)-2-oxopyrrolidin-1-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 247b)

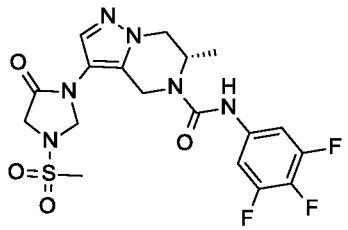
A mixture of (6S)-tert-butyl 3-(4-(hydroxymethyl)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **247a**, 500 mg, 1.43 mmol) and Dess-Martin periodinane (1.21 g, 2.85 mmol) in DCM (10 mL) was stirred at room temperature for 2 hours. Then the reaction mixture was filtered, and the filtrate was concentrated to give a crude product. The crude product was dissolved in MeOH (20 mL), to which was added K_2CO_3 (1.59 g, 11.5 mmol), and TOSMIC (1.12 g, 5.74 mmol). The reaction mixture was heated to 80 °C and stirred for 16 hours. The reaction mixture was concentrated in *vacuo*. The crude product was purified by flash chromatography (silica gel, 20% to 100% EtOAc in hexanes) to give compound **247a** as light yellow oil (80 mg). LCMS ($M+H^+$): 388.

Step 3: preparation of (6S)-6-methyl-3-(4-oxazol-5-yl-2-oxo-pyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 247)

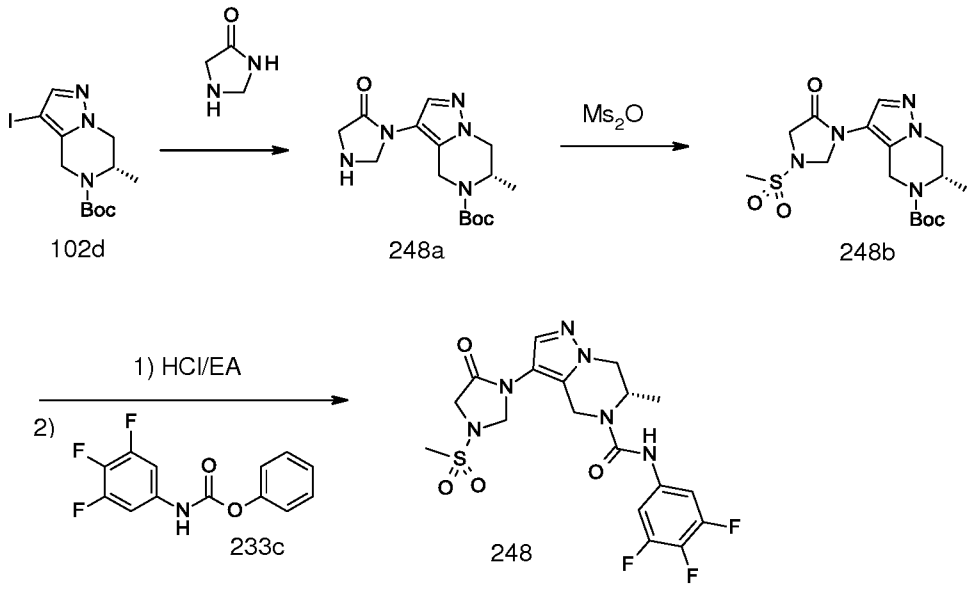
(6S)-Tert-butyl 6-methyl-3-(4-(oxazol-5-yl)-2-oxopyrrolidin-1-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **247b**, 80 mg, 206 μmol) was added to a solution of hydrogen chloride in EtOAc (1M, 10 mL). The reaction mixture was stirred at room temperature for 16 hours, then concentrated to give a white solid. To the solid was added DMF (3 mL), DIPEA (377 mg, 2.92 mmol) and phenyl (3,4,5-trifluorophenyl)carbamate (compound **233c**, 38.5 mg, 144 μmol). The resulting mixture was stirred at 40 °C for 3 hours, and then purified by prep-HPLC to give **Example 247** as white solid (12 mg). LCMS ($M+H^+$): 461. ^1H NMR (400MHz, chloroform-d) δ ppm 8.05 - 7.84 (m, 2H), 7.43 (d, *J*=7.8 Hz, 1H), 7.28 - 7.21 (m, 2H), 7.01 (d, *J*=9.8 Hz, 1H), 5.17 - 5.03 (m, 2H), 4.45 - 4.18 (m, 2.5H), 4.13 - 3.94 (m, 3H), 3.87 (d, *J*=9.8 Hz, 0.5H), 3.12 - 2.95 (m, 1H), 2.94 - 2.77 (m, 1H), 1.37 (d, *J*=7.0 Hz, 3H).

Example 248:

(6S)-6-methyl-3-(3-methylsulfonyl-5-oxo-imidazolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: preparation of (S)-tert-butyl 6-methyl-3-(5-oxoimidazolidin-1-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 248a)

A 20 mL microwave vial was charged with tert-butyl (6S)-3-iodo-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **102d**, 1 g, 2.75 mmol), imidazolidin-4-one (474 mg, 5.51 mmol), copper (I) iodide (105 mg, 551 μmol), potassium phosphate (1.17 g, 5.51 mmol),(1S,2S)-cyclohexane-1,2-diamine (126 mg, 1.1 mmol) and dioxane (15 mL). The vial was sealed and heated in microwave at 120 °C for 2.5 hours. The reaction mixture was filtered and the filtrate was concentrated in *vacuo* to give a crude product, which was purified by flash chromatography (silica gel, 0% to 80% EtOAc(contain 10% MeOH) in heptane) to give compound **248a** as light yellow oil (400 mg). LCMS ($M+H^+$): 322.

Step 2: preparation of (S)-tert-butyl 6-methyl-3-(3-(methylsulfonyl)-5-oxoimidazolidin-1-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 248b)

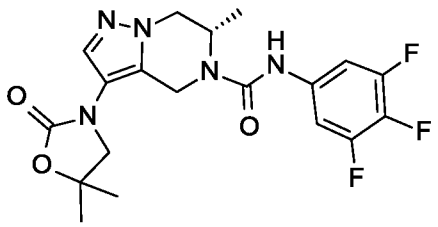
A mixture of (S)-tert-butyl 6-methyl-3-(5-oxoimidazolidin-1-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **248a**, 100 mg, 0.31 mmol), methanesulfonic anhydride (108 mg, 0.62 mmol) and N-ethyl-N-isopropylpropan-2-amine (201 mg, 1.56 mmol) in DCM (5 mL) was stirred at room temperature for 2 hours. The reaction mixture was concentrated in *vacuo*. The obtained residue was purified by flash chromatography (silica gel, 30% to 100% EtOAc (contain 10% Methanol) in hexanes) to give compound **248b** as a colorless oil (80 mg). LCMS ($M+H^+$): 400.

Step 3: preparation of (6S)-6-methyl-3-(3-methylsulfonyl-5-oxo-imidazolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 248)

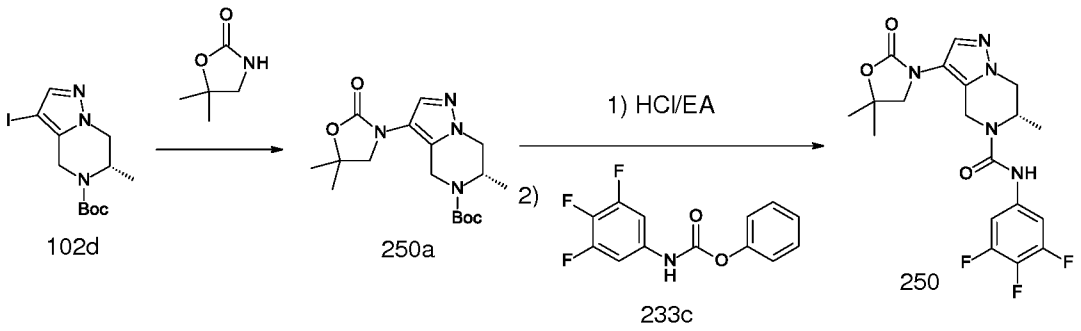
(S)-Tert-butyl 6-methyl-3-(3-(methylsulfonyl)-5-oxoimidazolidin-1-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **248b**, 80 mg, 200 μmol) was added to a solution of hydrogen chloride in EtOAc (1M, 10 mL), and the reaction mixture was stirred at room temperature for 16 hours. After removal of the solvent, the resulting light yellow solid was dissolved in DMF (5 mL), to which was added DIPEA (377 mg, 2.92 mmol) and phenyl (3,4,5-trifluorophenyl)carbamate (64.1 mg, 240 μmol). The reaction mixture was stirred at 40 °C for 3 hours, and then purified by prep-HPLC to give **Example 248** as a white solid (39 mg). LCMS ($M+H^+$): 473. ^1H NMR (400MHz, chloroform-d) δ ppm 7.48 (s, 1H), 7.42 (brs, 1H), 7.26 - 7.17 (m, 2H), 5.22 (d, *J*=6.0 Hz, 1H), 5.13 (d, *J*=6.3 Hz, 1H), 5.12-5.05 (m, 1H), 5.01 (d, J=16.6 Hz, 1H)4.42 (d, *J*=16.8 Hz, 1H), 4.32 (dd, *J*=5.1, 12.9 Hz, 1H), 4.26-4.15 (m, 2H), 4.09 (dd, *J*=1.6, 12.9 Hz, 1H), 3.08 (s, 3H), 1.38 (d, *J*=7.0 Hz, 3H).

Example 250:

(6S)-3-(5,5-dimethyl-2-oxo-oxazolidin-3-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:

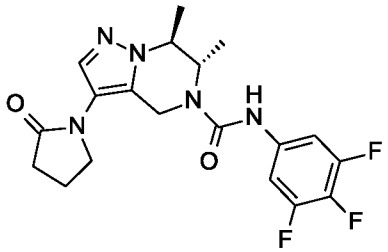


Preparation of (6S)-3-(5,5-dimethyl-2-oxo-oxazolidin-3-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 250)

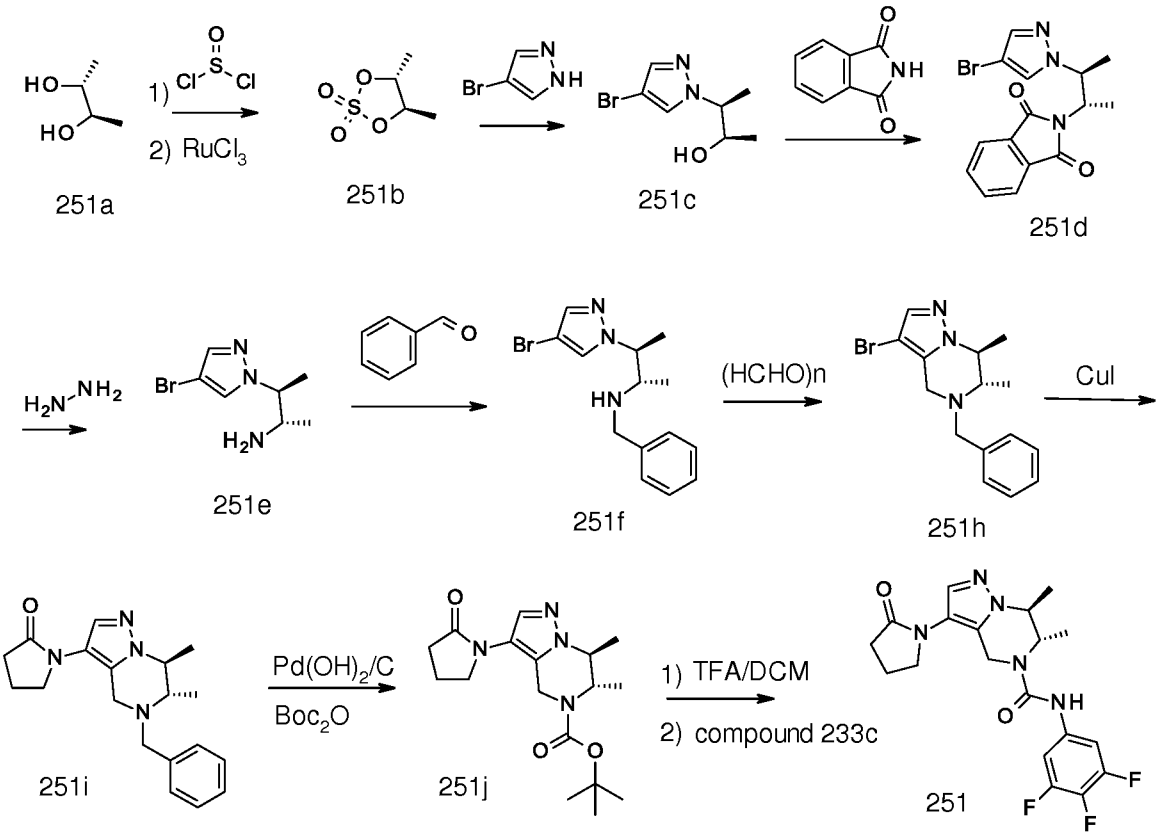
The title compound was prepared in analogy to Example **223** by using 5,5-dimethyloxazolidin-2-one instead of pyrrolidin-2-one and phenyl N-(3,4,5-trifluoro-phenyl)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). Example **250** was obtained as a white solid (110 mg). LCMS ($M+H^+$): 424. ^1H NMR (400MHz, MeOD) δ ppm 7.65 (s, 1H), 7.31-7.27 (m, 2H), 5.07 (d, *J*=16.8 Hz, 1H), 5.01 - 4.94 (m, 1H), 4.55 (d, *J*=16.8 Hz, 1H), 4.30 (dd, *J*=4.4, 12.9 Hz, 1H), 4.20 - 4.11 (m, 1H), 3.89 - 3.75 (m, 2H), 1.58 (s, 6H), 1.27 (d, *J*=6.8 Hz, 3H).

Example 251:

(6S,7S)-6,7-dimethyl-3-(2-oxopyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: Preparation of (4R,5R)-4,5-dimethyl-1,3,2-dioxathiolane 2,2-dioxide (compound 251b)

A solution of $SOCl_2$ (7.26 g, 4.45 mL, 61 mmol) in DCM (50 mL) was added dropwise to a stirred mixture of (2R,3R)-butane-2,3-diol (5 g, 55.5 mmol), imidazole (18.9 g, 277 mmol) and triethylamine (19.6 g, 27.1 mL, 194 mmol) in DCM (200 mL) at 0 °C, and the reaction mixture was stirred for 1 hour at 0 °C. The reaction mixture was quenched with H_2O and extracted twice with DCM. The combined organic layer was washed with H_2O, dried over $MgSO_4$, filtered and concentrated to give a residue. To a stirred solution of the crude residue in acetonitrile (200 mL) at 0 °C were added sodium periodate (17.8 g, 83.2 mmol), water (150 mL) and rhodium (III) chloride (1.16 g, 5.55 mmol) sequentially and the reaction mixture was stirred at 0 °C for 3 hours. The two layers were separated and the aqueous layer was extracted three times with EtOAc. The combined organic layer was washed with saturated aqueous $NaHCO_3$ and brine, and then dried over $MgSO_4$, filtered and concentrated to give compound **251b** as a colorless oil (8 g).

Step 2: Preparation of (2R,3S)-3-(4-bromo-1H-pyrazol-1-yl)butan-2-ol (compound 251c)

A mixture of (4R,5R)-4,5-dimethyl-1,3,2-dioxathiolane 2,2-dioxide (compound **251b**, 8 g, 52.6 mmol), 4-bromo-1H-pyrazole (11.6 g, 78.9 mmol) and Cs_2CO_3 (34.3 g, 105 mmol) in DMF (50 mL) was stirred at room temperature for 16 hours. The reaction mixture was filtered and concentrated. The resulting residue was taken up in 400 mL of 1:2 THF: 50% aq. H_2SO_4, and stirred vigorously for 48 hours. The reaction mixture was then carefully basified with 10 M NaOH, and the layers were separated. The aqueous layer was extracted twice with DCM, and the combined organic layer was washed with brine, dried over $MgSO_4$, filtered and concentrated to give compound **251c** as a colorless oil (8 g). LCMS ($M+H^+$): 219

Step 3: Preparation of 2-((2S,3S)-3-(4-bromo-1H-pyrazol-1-yl)butan-2-yl)isoindoline-1,3-dione (compound 251d)

To a mixture of (2R,3S)-3-(4-bromo-1H-pyrazol-1-yl)butan-2-ol (compound **251c**, 8 g, 36.5 mmol), isoindoline-1,3-dione (5.91 g, 40.2 mmol) and triphenylphosphine (12.5 g, 47.5 mmol) in THF (75 mL) was added DIAD (11.1 g, 54.8 mmol) dropwise at room temperature. Then the reaction mixture was stirred at room temperature for 2 hours, and concentrated in *vacuo*. The crude product was purified by flash chromatography (silica gel, 0% to 50% EtOAc in hexanes) to give compound **251d** as a white solid (5 g). LCMS ($M+H^+$): 348

Step 4: Preparation of (2S,3S)-3-(4-bromo-1H-pyrazol-1-yl)butan-2-amine (compound 251e)

A mixture of 2-((2S,3S)-3-(4-bromo-1H-pyrazol-1-yl)butan-2-yl)isoindoline-1,3-dione (compound **251d**, 5 g, 14.4 mmol) and Hydrazine hydrate (7.19 g, 144 mmol) in MeOH (50 mL) was stirred at 80 °C for 15 hours. The reaction mixture was concentrated in vacuo. The residue was dissolved in DCM, the solid was filtered off and the filtrate was concentrated to give compound **251e** as a slight yellow oil (3 g). LCMS ($M+H^+$): 218

Step 5: Preparation of (2S,3S)-N-benzyl-3-(4-bromo-1H-pyrazol-1-yl)butan-2-amine (compound 251f)

A mixture (2S,3S)-3-(4-bromo-1H-pyrazol-1-yl)butan-2-amine (compound **251e**, 3 g, 13.8 mmol) and benzaldehyde (1.61 g, 15.1 mmol) in MeOH (50 mL) was stirred for 2 hours at room temperature. Then sodium borohydride (624 mg, 16.5 mmol) was added slowly at 0 °C in 30 mins and the reaction mixture was stirred at room temperature for another 30 mins. The reaction mixture was poured into 100 mL of H_2O and extracted with EtOAc (100 mL) twice. The organic layers were combined, dried over Na_2SO_4 and then concentrated in *vacuo*. The crude product was purified by flash chromatography (silica gel, 0% to 50% EtOAc in hexanes) to give compound **251f** as light yellow oil (4 g). LCMS ($M+H^+$): 308

Step 6: Preparation of (6S,7S)-5-benzyl-3-bromo-6,7-dimethyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound 251h)

To a stirred solution of (2S,3S)-N-benzyl-3-(4-bromo-1H-pyrazol-1-yl)butan-2-amine (compound **251d**, 4 g, 13 mmol) in acetonitrile (50 mL) was added paraformaldehyde (1.95 g, 64.9 mmol) and 2,2,2-trifluoroacetic acid (296 mg, 2.6 mmol), and the reaction mixture was stirred at 70 °C for 6 hours. The reaction mixture was concentrated and the residue was then taken up in EtOAc, and washed with $NaHCO_3$ aq. solution and brine. The organic layer was concentrated and the residue was purified on a silica gel column (heptane: EtOAc 1:0 to 9:1) to give compound **251h** as a colorless oil (2.3 g). LCMS ($M+H^+$): 320

Step 7: Preparation of 1-((6S,7S)-5-benzyl-6,7-dimethyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)pyrrolidin-2-one (compound 251i)

A 10 mL microwave vial was charged with (6S,7S)-5-benzyl-3-bromo-6,7-dimethyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **251h**, 300 mg, 0.94 mmol), copper (I) iodide (35.7 mg, 0.19 mmol), potassium carbonate (388 mg, 2.81 mmol), pyrrolidin-2-one (159 mg, 1.87 mmol), N1,N2-dimethylethane-1,2-diamine (33 mg, 0.38 mmol), and dioxane (5 mL). The vial was sealed and heated in microwave at 125 °C for 2 hours. The reaction mixture was poured into 20 mL of H_2O and extracted with EtOAc (20 mL) twice. The organic layers were combined, dried, and then concentrated in *vacuo*. The crude product was purified by flash

chromatography (silica gel, 20% to 50% EtOAc in hexanes, where EtOAc contains 10% MeOH) to give compound **251i** (200 mg) as a colorless oil. LCMS ($M+H^+$): 325

Step 8: Preparation of (6S,7S)-tert-butyl 6,7-dimethyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 251j)

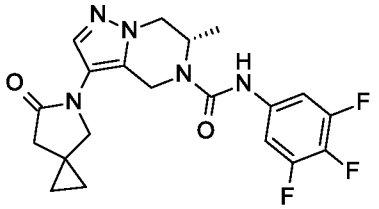
A mixture of 1-((6S,7S)-5-benzyl-6,7-dimethyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)pyrrolidin-2-one (compound **251i**, 200 mg, 616 μmol), Boc_2O(402 mg, 1.8 mmol) and $Pd(OH)_2/C$ (43.3 mg, 61.6 μmol) in EtOH (50 mL) was stirred at 50 °C for 16 hours under hydrogen. The reaction mixture was filtered through celite. The filtrate was concentrated to give compound **251j** (200 mg) as a colorless oil. LCMS ($M+H^+$): 335

Step 9: Preparation of (6S,7S)-6,7-dimethyl-3-(2-oxopyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 251)

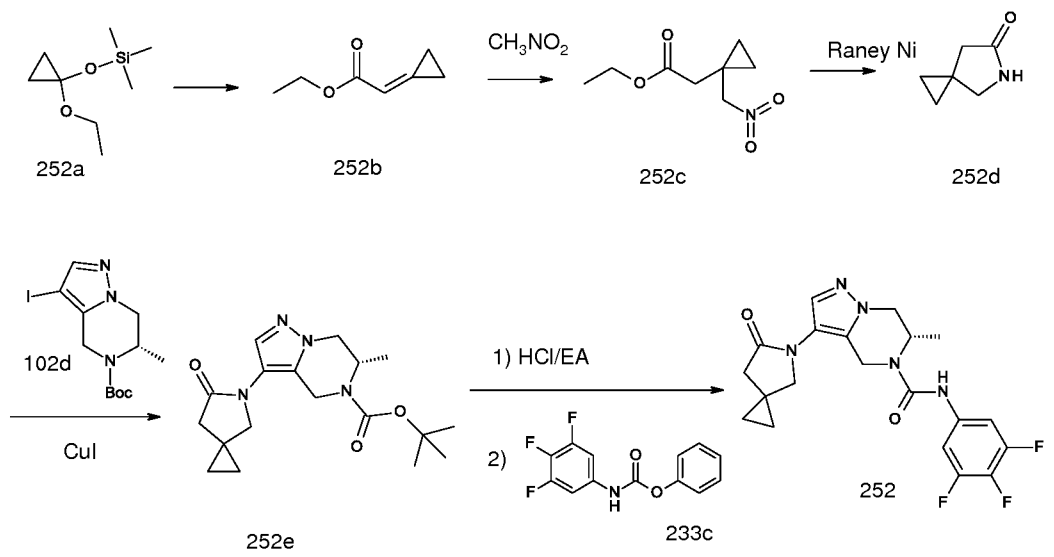
A solution of (6S,7S)-tert-butyl 6,7-dimethyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **251j**, 200 mg, 0.60 mmol) in 2,2,2-trifluoroacetic acid (2 mL) and DCM (2 mL) was stirred at room temperature for 30 mins. The reaction mixture was concentrated, and the residue was dissolved in DMF (5 mL), to which was added N-ethyl-N-isopropylpropan-2-amine (386 mg, 2.99 mmol) and phenyl (3,4,5-trifluorophenyl)carbamate (192 mg, 0.72 mmol). The reaction mixture was stirred at 70 °C for 0.5 hours. The reaction mixture was diluted with EtOAc (30 mL), and washed with water. The organic layer was dried and concentrated, and the residue was purified by flash chromatography to give Example **251** (100 mg) as a white powder. LCMS ($M+H^+$): 408. ^1H NMR (400MHz, MeOD) δ ppm 7.64 (s, 1H), 7.36 - 7.25 (m, 2H), 5.06 (d, *J*=16.8 Hz, 1H), 4.82 - 4.73 (m, 1H), 4.50 (d, *J*=16.8 Hz, 1H), 4.41 - 4.33 (m, 1H), 3.92 - 3.80 (m, 2H), 2.61 - 2.52 (m, 2H), 2.25 (q, *J*=7.6 Hz, 2H), 1.45 (d, *J*=6.8 Hz, 3H), 1.25 (d, *J*=7.0 Hz, 3H).

Example 252:

(6S)-6-methyl-3-(6-oxo-5-azaspiro[2.4]heptan-5-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of 5-azaspiro[2.4]heptan-6-one (compound252d)

Step 1: A solution of (1-ethoxycyclopropoxy)trimethylsilane (compound **252a**, 50 g, 287 mmol) in MeOH (150 mL) was stirred at 20 °C for 1 hour and then concentrated under reduced pressure. The residue was dissolved in toluene (500 mL). To the above solution was added benzoic acid (7.0 g, 57.4 mmol). The mixture was heated to 90 °C with stirring, then a solution of (carbethoxymethylene)triphenylphosphorane (100 g, 287 mmol) in toluene (1200 mL) was added at the same temperature. The resulting mixture was stirred at 90 °C for 16 hours, and then concentrated under reduced pressure. The residue was purified by column chromatography to give ethyl 2-cyclopropylideneacetate (compound **252b**, 6 g) as a colorless oil.

Step 2: To a solution of ethyl 2-cyclopropylideneacetate (compound **252b**, 5.0 g, 39.7 mmol) in nitromethane (50 mL) and THF (50 mL) was added DBU (4.96 g, 19.8 mmol). The mixture was stirred at room temperature for 16 hours, and then concentrated under reduced pressure. The residue was purified by column chromatography to give compound **252c** as a colorless oil (3.5 g).

Step 3: A mixture of ethyl 2-[1-(nitromethyl)cyclopropyl]acetate (compound **252c**, 3.5 g, 18.7 mmol) and Raney Ni (500 mg) in MeOH (70 mL) was stirred at 50 °C under 50 psi of hydrogen for 16 hours. The mixture was filtered and the filtrate was concentrated under reduced pressure. The residue was triturated with methyl tert-butyl ether and PE to give compound **252d** as a white solid (850 mg). LCMS ($M+H^+$): 112.

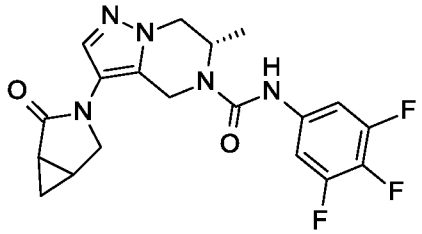
Preparation of (6S)-6-methyl-3-(6-oxo-5-azaspiro[2.4]heptan-5-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 252)

The title compound was prepared in analogy to Example **223** by using 5-azaspiro[2.4]heptan-6-one (compound **252d**) instead of pyrrolidin-2-one and phenyl N-(3,4,5-trifluorophenyl)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-

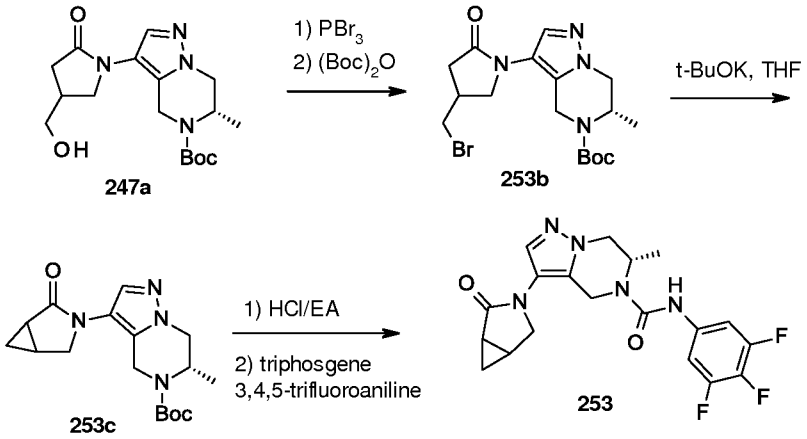
pyridyl]carbamate (compound **218c**). Example **252** was obtained as a white solid (30 mg). LCMS ($M+H^+$): 420. ^1H NMR (400 MHz, $CDCl_3$) δ ppm 8.07 (s, 1H), 7.40 (s, 1H), 7.30 (s, 2H), 5.21 - 5.02 (m, 2H), 4.42 - 4.26 (m, 2H), 4.01 (dd, 1H), 3.92 (d, 1H), 3.57 (d, 1H), 2.79 - 2.69 (m, 1H), 2.63 - 2.52 (m, 1H), 1.42 (d, 3H), 0.91 - 0.74 (m, 4H).

Example 253:

(6S)-6-methyl-3-(2-oxo-3-azabicyclo[3.1.0]hexan-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: preparation of tert-butyl (6S)-3-[4-(bromomethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 253b)

To a solution of tert-butyl (6S)-3-[4-(hydroxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **247a**, 50.0 mg, 0.14 mmol) in toluene (5.0 mL) was added dropwise PBr_3 (43.0 mg, 0.16 mmol) at 0 °C, then the reaction mixture was stirred at 80 °C for 12 hours. The reaction was quenched by H_2O (20 mL) and extracted with EtOAc (50 mL) twice. The organic phases were combined and concentrated in *vacuo* to give a crude product. To a solution of the crude product (40.0 mg, 0.11 mmol) in dioxane (5.0 mL) was added $(Boc)_2O$ (28.34 mg, 0.13 mmol) and a solution of $NaHCO_3$ (10 mg) in H_2O (5.0 mL), and then the reaction mixture was stirred at room temperature for 12 hours. The

reaction mixture was concentrated and the residue was purified by prep-HPLC to give compound **253b** (20 mg). LCMS ($M+H^+$): 413.

Step 2: preparation of tert-butyl (6S)-6-methyl-3-(2-oxo-3-azabicyclo[3.1.0]hexan-3-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 253c)

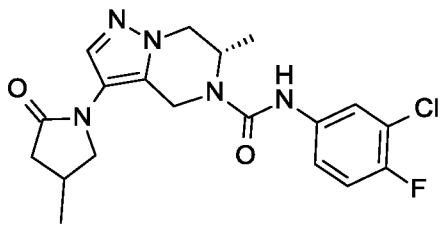
To a solution of tert-butyl (6S)-3-[4-(bromomethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **253b**, 20 mg, 0.05 mmol) in THF (5 mL) was added a solution of t-BuOK in THF (0.1 mL, 1.0 mol/L) at 0 °C, and then the reaction mixture was stirred at room temperature for 4 hours. Then H_2O (10 mL) and EtOAc (50 mL) were added, and the organic phase was separated and concentrated to provide compound **253c** (20 mg). LCMS ($M+H^+$): 333.

Step 3: Preparation of (6S)-6-methyl-3-(2-oxo-3-azabicyclo[3.1.0]hexan-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 253)

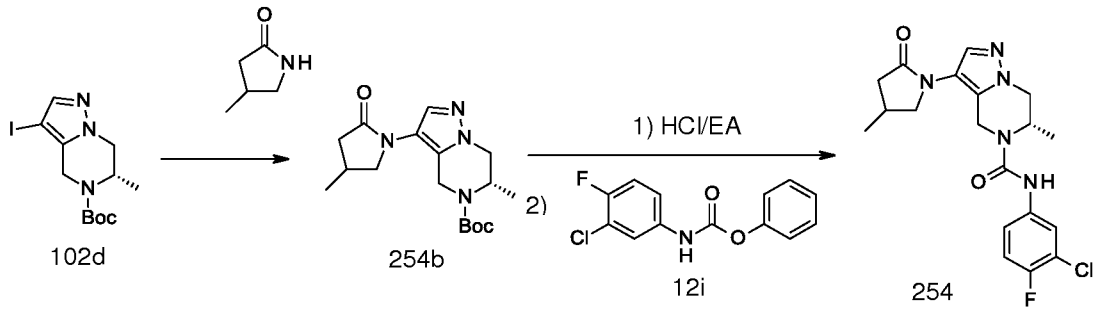
The title compound was prepared in analogy to the preparation of Example **11** by 3,4,5-trifluoroaniline instead of 3-(trifluoromethyl)aniline and tert-butyl (6S)-6-methyl-3-(2-oxo-3-azabicyclo[3.1.0]hexan-3-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **253c**) instead of tert-butyl 3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **11a**). Example **253** was obtained as a white solid. LCMS ($M+H^+$): 406. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.09 (s, 0.5H), 9.08 (s, 0.5H), 7.55 (s, 0.5H), 7.54 (s, 0.5H) 7.46 - 7.38 (m, 2H), 4.98 - 4.79 (m, 2H), 4.32 (d, *J*=17.1 Hz, 1H), 4.21 - 4.13 (m, 1H), 4.12 - 4.07 (m, 1H), 3.98 (dd, *J*=6.0, 10.0 Hz, 1H), 3.89 (dd, *J*=5.9, 10.2 Hz, 1H), 2.04 (br. s., 1H), 1.93 (br. s., 1H), 1.22 - 1.06 (m, 4H), 0.77 - 0.71 (m, 1H).

Example 254:

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(4-methyl-2-oxo-pyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:

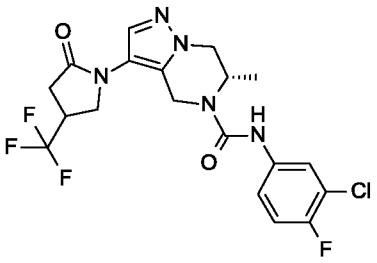


Preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(4-methyl-2-oxo-pyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 254)

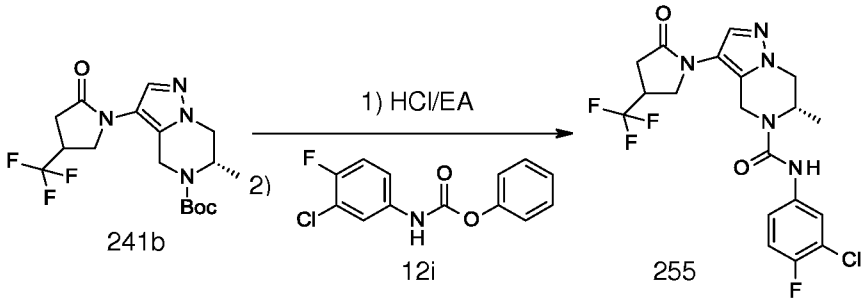
The title compound was prepared in analogy to Example **223** by using 4-methylpyrrolidin-2-one instead of pyrrolidin-2-one, and phenyl N-(3-chloro-4-fluoro-phenyl)carbamate (compound **12i**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 254** was obtained as a solid (48 mg). LCMS ($M+H^+$): 406. ^{1}H NMR (400MHz, MeOD) δ ppm 7.67 - 7.56 (m, 2H), 7.38 - 7.32 (m, 1H), 7.22 - 7.12 (m, 1H), 5.08 - 4.94 (m, 2H), 4.56 - 4.45 (m, 1H), 4.33 - 4.26 (m, 1H), 4.20 - 4.11 (m, 1H), 4.00 - 3.94 (m, 1H), 3.51 – 3.44 (m, 1H), 2.76 - 2.62 (m, 2H), 2.27 - 2.17 (m, 1H), 1.30 - 1.20 (m, 6H).

Example 255:

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-[2-oxo-4-(trifluoromethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



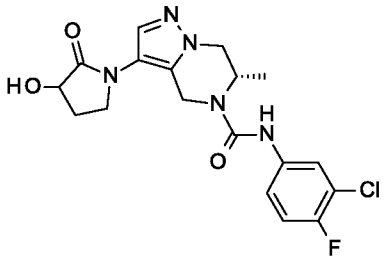
Preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-[2-oxo-4-(trifluoromethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

(Example 255)

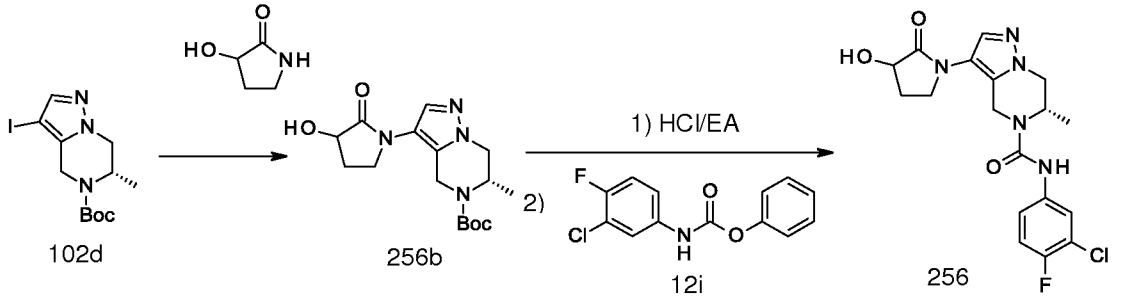
The title compound was prepared in analogy to Example **223** by using 4-(trifluoromethyl)pyrrolidin-2-one instead of pyrrolidin-2-one, and phenyl N-(3-chloro-4-fluoro-phenyl)carbamate (compound **12i**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 255** was obtained as a white solid (21 mg). LCMS ($M+H^+$): 460. ^1H NMR (400MHz, MeOD) δ ppm 7.66 (s, 1H), 7.64 - 7.58 (m, 1H), 7.37 - 7.31 (m, 1H), 7.21 - 7.13 (m, 1H), 5.09 - 4.92 (m, 2H), 4.52 - 4.45 (m, 1H), 4.32 - 4.28 (m, 1H), 4.21 - 4.07 (m, 2H), 3.98 - 3.94 (m, 1H), 3.58 - 3.45 (m, 1H), 2.98 - 2.85 (m, 1H), 2.74 - 2.68 (m, 1H), 1.29 - 1.26 (m, 3H)

Example 256:

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(3-hydroxy-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



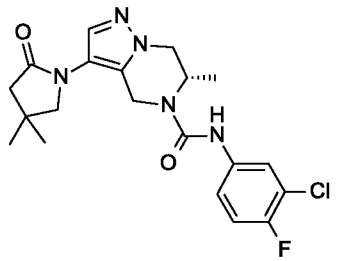
Preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-3-(3-hydroxy-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 256)

The title compound was prepared in analogy to Example **223** by using 3-hydroxylpyrrolidin-2-one instead of pyrrolidin-2-one and phenyl N-(3-chloro-4-fluoro-phenyl)carbamate (compound **12i**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 256** was obtained as a solid (18 mg). LCMS ($M+H^+$): 408. ^1H NMR (400MHz, MeOD) δ ppm 7.65 (s, 1H), 7.63 (dd, *J*=2.5, 6.8 Hz, 1H), 7.37 - 7.33 (m, 1H), 7.17 (t, *J*=8.9 Hz, 1H), 5.03 (d, *J*=17.1 Hz, 1H), 4.99 – 4.97 (m, 1H), 4.58 (d, *J*=17.1 Hz, 1H), 4.47 (t,

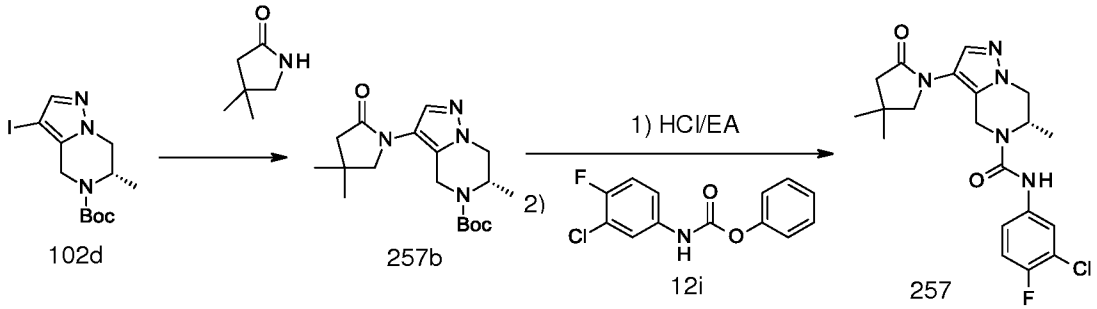
J=8.4 Hz, 1H), 4.30 (dd, *J*=4.4, 12.7 Hz, 1H), 4.17 (dd, *J*=1.0, 12.8 Hz, 1H), 3.85 - 3.70 (m, 2H), 2.64 - 2.52 (m, 1H), 2.14 - 2.02 (m, 1H), 1.29 (d, *J*=7.0 Hz, 3H)

Example 257:

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4,4-dimethyl-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:

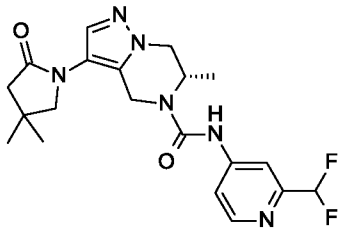


Preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4,4-dimethyl-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 257)

The title compound was prepared in analogy to Example **223** by using 4,4-dimethylpyrrolidin-2-one instead of pyrrolidin-2-one and phenyl N-(3-chloro-4-fluoro-phenyl)carbamate (compound **12i**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 257** was obtained as a solid (5 mg). LCMS ($M+H^+$): 420. ^{1}H NMR (400MHz, MeOD) δ ppm 7.65 - 7.59 (m, 2H), 7.34 - 7.31(m, 1H), 7.17 (t, *J*=8.9 Hz, 1H), 5.04 (d, *J*=16.8 Hz, 1H), 5.00 - 4.93 (m, 1H), 4.51 (d, *J*=17.1 Hz, 1H), 4.30 (dd, *J*=4.5, 12.8 Hz, 1H), 4.16 (dd, *J*=1.1, 12.7 Hz, 1H), 3.66 - 3.53 (m, 2H), 2.41 (s, 2H), 1.32 - 1.23 (m, 9H)

Example 258:

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-3-(4,4-dimethyl-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

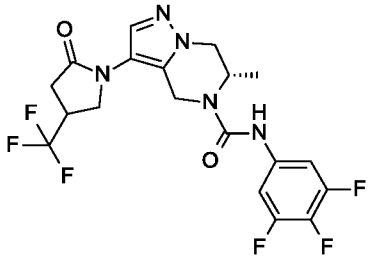


Preparation of (6S)-N-[2-(difluoromethyl)-4-pyridyl]-3-(4,4-dimethyl-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 258)

The title compound was prepared in analogy to Example **223** by using 4,4-dimethylpyrrolidin-2-one instead of pyrrolidin-2-one. **Example 258** was obtained as a solid (5 mg). LCMS ($M+H^+$): 419. ^1H NMR (400MHz, MeOD) δ ppm 8.43 (d, *J*=5.5 Hz, 1H), 7.87 (d, *J*=2.0 Hz, 1H), 7.68 (dd, *J*=2.3, 5.8 Hz, 1H), 7.62 (s, 1H), 6.67 (t, *J*=54 Hz, 1H), 5.10 (d, *J*=17.1 Hz, 1H), 5.05 - 4.97 (m, 1H), 4.55 (d, *J*=16.8 Hz, 1H), 4.33 (dd, *J*=4.3, 12.8 Hz, 1H), 4.18 (d, *J*=14.1 Hz, 1H), 3.66 - 3.56 (m, 2H), 2.42 (s, 2H), 1.33 - 1.25 (m, 9H)

Example 259:

(6S)-6-methyl-3-[2-oxo-4-(trifluoromethyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

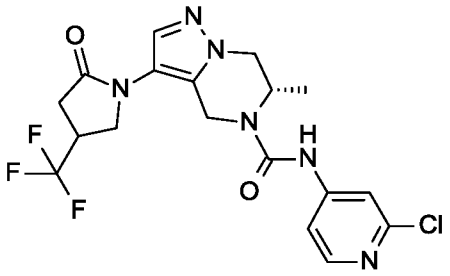


Preparation of 6S)-6-methyl-3-[2-oxo-4-(trifluoromethyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide（Example 259）

The title compound was prepared in analogy to Example **223** by using 4-(trifluoromethyl)pyrrolidin-2-one instead of pyrrolidin-2-one and phenyl N-[3,4,5-trifluoro-phenyl]carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 259** was obtained as a white solid (38 mg). LCMS ($M+H^+$): 462. ^1H NMR (400MHz, MeOD) δ ppm 7.66 (s, 1H), 7.33 - 7.23 (m, 2H), 5.09 - 4.92 (m, 2H), 4.52-4.46 (m, 1H), 4.32 - 4.28 (m, 1H), 4.21 - 4.07 (m, 2H), 4.00 - 3.89 (m, 1H), 3.57 - 3.45 (m, 1H), 2.98 - 2.86 (m, 1H), 2.74 - 2.69 (m, 1H), 1.29 - 1.26 (m, 3H)

Example 260:

(6S)-N-(2-chloro-4-pyridyl)-6-methyl-3-[2-oxo-4-(trifluoromethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

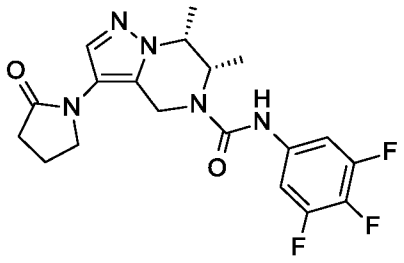


Preparation of (6S)-N-(2-chloro-4-pyridyl)-6-methyl-3-[2-oxo-4-(trifluoromethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide（Example 260）

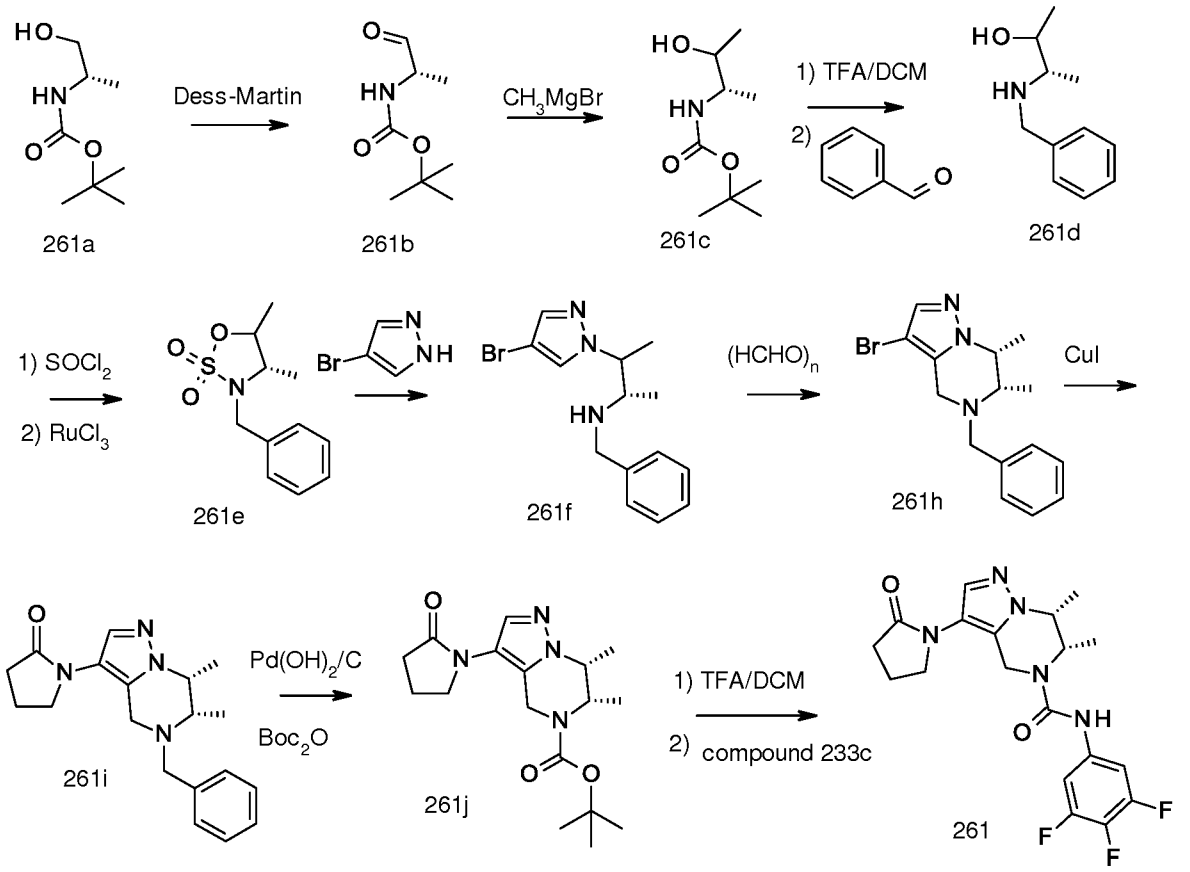
The title compound was prepared in analogy to Example **223** by using 4-(trifluoromethyl)pyrrolidin-2-one instead of pyrrolidin-2-one and phenyl N-(2-chloro-4-pyridyl)carbamate instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). Example **260** was obtained as a white solid (18 mg). LCMS ($M+H^+$): 443. ^1H NMR (400MHz, MeOD) δ ppm 8.15 (d, *J*=5.8 Hz, 1H), 7.72 - 7.64 (m, 2H), 7.47 - 7.45 (m, 1H), 5.11 - 5.04 (m, 1H), 4.99 - 4.95 (m, 1H), 4.55 - 4.52 (m, 1H), 4.38 - 4.27 (m, 1H), 4.17 - 4.06 (m, 2H), 3.97 - 3.93 (m, 1H), 3.56 - 3.46 (m, 1H), 2.98 - 2.85 (m, 1H), 2.78 - 2.66 (m, 1H), 1.31 - 1.28 (m, 3H)

Example 261:

(6S,7R)-6,7-dimethyl-3-(2-oxopyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: preparation of (S)-tert-butyl (1-oxopropan-2-yl)carbamate (compound 261b)

To a solution of (S)-tert-butyl (1-hydroxypropan-2-yl)carbamate (compound **261a**, 8.76 g, 50 mmol) in DCM (200 mL) was added Dess-Martin periodinane (31.8 g, 75 mmol) slowly. After stirred at room temperature for 2 hours, the reaction mixture was filtered through silica gel. The filtrate was concentrated in vacuo to give compound **261b** as a colorless oil (10 g).

Step 2: preparation of tert-butyl ((2S)-3-hydroxybutan-2-yl)carbamate (compound 261c)

To a solution of (S)-tert-butyl (1-oxopropan-2-yl)carbamate (compound **261b**, 8.66 g, 50 mmol) in THF (100 mL) was added methylmagnesium bromide (150 mL, 150 mmol) slowly at -78 °C. The reaction mixture was stirred at -78 °C for 2 hours and then quenched with water. The reaction mixture was poured into 200 mL brine and extracted with EtOAc (100 mL) twice. The organic layers were combined, dried and concentrated in *vacuo* to give crude compound **261c** as a colorless oil (9 g). LCMS ($M+H^+$): 190

Step 3: preparation of tert-butyl (3S)-3-(benzylamino)butan-2-ol (compound 261d)

A mixture of tert-butyl ((2S)-3-hydroxybutan-2-yl)carbamate (compound **261c**, 8 g, 25.4 mmol) and trifluoroacetic acid (28.9 g, 19.5 mL, 254 mmol) in DCM (40 mL) was stirred at room temperature for 1 hour. The reaction mixture was concentrated in *vacuo* and the residue

was dissolved in DCM (100 mL), to which benzaldehyde (2.69 g, 25.4 mmol) and sodium triacetoxyborohydride (10.8 g, 50.7 mmol) were added. The reaction mixture was stirred at room temperature for 16 hours. Then the reaction mixture was poured into 250 mL saturated aqueous $NaHCO_3$ and extracted with EtOAc (200 mL) twice. The combined organic phase was dried over Na_2SO_4 and concentrated in *vacuo*. The crude product was purified by flash chromatography (silica gel, 20% to 80% EtOAc in hexanes) to give compound **261d** as a light yellow oil (2 g). LCMS ($M+H^+$): 180.

Step 4: preparation of (5S)-3-benzyl-4,5-dimethyl-1,2,3-oxathiazolidine 2,2-dioxide (compound 261e)

A solution of $SOCl_2$ (1.46 g, 896 μL, 12.3 mmol) in DCM (10 mL) was added dropwise to a stirred mixture of (3S)-3-(benzylamino)butan-2-ol (compound **261d**, 2 g, 11.2 mmol), imidazole (3.8 g, 55.8 mmol) and triethylamine (3.95 g, 39 mmol) in DCM (50 mL) at 0 °C, and the reaction mixture was allowed to stirred at 0 °C for 1 hour. The reaction mixture was quenched with H_2O and extracted twice with DCM. The combined organic layer was washed with H_2O, dried over $MgSO_4$, filtered and concentrated. To a stirred solution of the crude residue in acetonitrile (100 mL) at 0 °C were added sodium periodate (3.82 g, 17.9 mmol), water (75 mL) and rhodium (III) chloride (233 mg, 1.12 mmol) sequentially and the reaction mixture was stirred at 0 °C for 3 hours. The two layers were separated and the aqueous layer was extracted three times with EtOAc. The combined organic layer was washed with saturated aqueous $NaHCO_3$ and brine, the organic layer was dried over $MgSO_4$, filtered and concentrated to give compound **261e** as a colorless oil (3 g), LCMS ($M+H^+$): 242.

Step 5: preparation of (2S)-N-benzyl-3-(4-bromo-1H-pyrazol-1-yl)butan-2-amine (compound 261f)

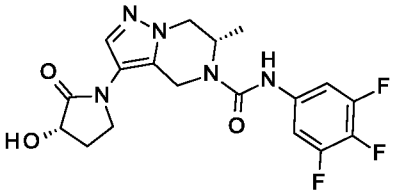
A mixture of (5S)-3-benzyl-4,5-dimethyl-1,2,3-oxathiazolidine 2,2-dioxide (compound **261e**, 3 g, 10.6 mmol), 4-bromo-1H-pyrazole (3.11 g, 21.1 mmol) and Cs_2CO_3 (6.89 g, 21.1 mmol) in DMF (50 mL) was stirred at room temperature for 16 hours. The reaction mixture was filtered and concentrated. The residue was dissolved in DCM and 20% aq.H_2SO_4 (150 mL, 1:1) and stirred vigorously for 12 hours. The reaction mixture was then carefully basified with 10 M NaOH, the layers were separated. The aqueous layer was extracted twice with DCM, and the combined organic layer was washed with brine, dried over $MgSO_4$, filtered and concentrated. The crude product was purified by flash chromatography (silica gel, 20% to 60% EtOAc in hexanes) to give compound **261f** as a colorless oil (1 g). LCMS ($M+H^+$): 308

Preparation of (6S,7R)-6,7-dimethyl-3-(2-oxopyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 261)

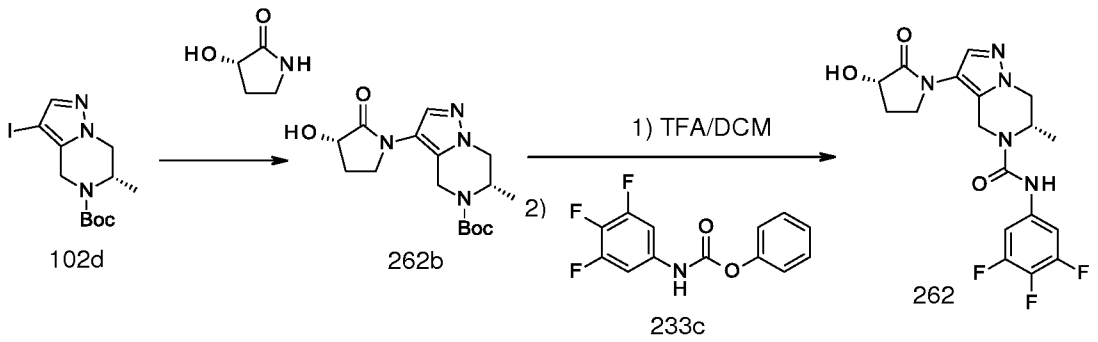
The title compound was prepared in analogy to **Example 251** by using (2S)-N-benzyl-3-(4-bromo-1H-pyrazol-1-yl)butan-2-amine (compound **261f**) instead of (2S,3S)-3-(4-bromo-1H-pyrazol-1-yl)butan-2-amine (compound **251e**). Example **261** was obtained as a white solid (12 mg). LCMS ($M+H^+$): 408. ^{1}H NMR (400MHz, MeOD) δ ppm 7.62 (s, 1H), 7.32-7.26 (m, 2H), 5.00 (d, *J*=16.8 Hz, 2H), 4.79 - 4.71 (m, 1H), 4.50 (d, *J*=16.8 Hz, 1H), 4.46 - 4.39 (m, 1H), 3.93 - 3.80 (m, 2H), 2.60 - 2.52 (m, 2H), 2.29 - 2.21 (m, 2H), 1.62 (d, *J*=6.8 Hz, 3H), 1.16 (d, *J*=6.8 Hz, 3H).

Example 262:

(6S)-3-[(3S)-3-hydroxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of (6S)-3-[(3S)-3-hydroxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 262)

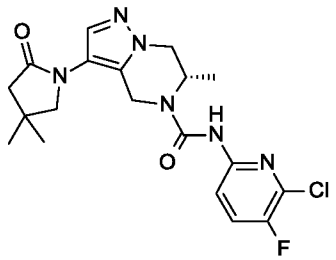
Step 1: To a 25 mL microwave vial was added (S)-tert-butyl 3-iodo-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (150 mg, 413 μmol), (S)-3-hydroxypyrrolidin-2-one (83.5 mg, 826 μmol), copper (I) iodide (15.7 mg, 82.6 μmol), potassium phosphate (175 mg, 826 μmol) and (1S,2S)-cyclohexane-1,2-diamine (18.9 mg, 165 μmol) in dioxane (15 mL). The vial was capped and heated in the microwave at 120 °C for 2.5 hours. The reaction mixture was filtered and the filtrate was concentrated in *vacuo* to give crude

product, which was purified by flash chromatography (silica gel) to give compound **262b** as a light brown oil (200 mg). LCMS ($M+H^+$): 337.

Step 2: A mixture of (S)-tert-butyl 3-((S)-3-hydroxy-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (200 mg, 595 μmol) in DCM (10 mL) and TFA (5 mL) was stirred at room temperature for 30 minutes. The reaction mixture was concentrated, and the residue was dissolved in DMF (3 mL), to which was added N-ethyl-N-isopropylpropan-2-amine (384 mg, 2.97 mmol) and phenyl (3,4,5-trifluorophenyl)carbamate (191 mg, 713 μmol). The reaction mixture was stirred at 70 °C for 0.5 hours. Then the reaction mixture was diluted with ethyl acetate (30 mL), and washed with water. The organic layer was dried and concentrated. The crude material was purified by preparative HPLC to give **Example 262** as a white solid (12 mg). LCMS ($M+H^+$): 410. ^{1}H NMR (400MHz, MeOD) δ ppm 7.65 (s, 1H), 7.33-7.26 (m, 2H), 5.03 (d, *J*=17.1 Hz, 1H), 4.99 - 4.95 (m, 1H), 4.58 (d, *J*=17.1 Hz, 1H), 4.47 (t, *J*=8.4 Hz, 1H), 4.35 - 4.26 (m, 1H), 4.16 (dd, *J*=1.0, 12.8 Hz, 1H), 3.84 - 3.72 (m, 2H), 2.61-2.57 (m, 1H), 2.16 - 2.00 (m, 1H), 1.29 (d, *J*=7.0 Hz, 3H).

Example 263:

(6S)-N-(6-chloro-5-fluoro-2-pyridyl)-3-(4,4-dimethyl-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

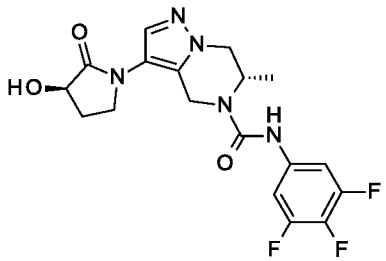


Preparation of (6S)-N-(6-chloro-5-fluoro-2-pyridyl)-3-(4,4-dimethyl-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 263)

The title compound was prepared in analogy to Example **223** by using 4,4-dimethylpyrrolidin-2-one instead of pyrrolidin-2-one and phenyl N-(6-chloro-5-fluoro-2-pyridyl)carbamate (compound **140d**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 263** was obtained as a solid (22 mg). LCMS ($M+H^+$): 421. ^{11}H NMR (400MHz, MeOD) δ ppm 7.83 (dd, *J*=3.0, 8.8 Hz, 1H), 7.71 - 7.59 (m, 2H), 5.07 (d, *J*=16.8 Hz, 1H), 5.03 - 4.96 (m, 1H), 4.52 (d, *J*=17.1 Hz, 1H), 4.30 (dd, *J*=4.4, 12.7 Hz, 1H), 4.16 (dd, *J*=1.0, 12.8 Hz, 1H), 3.66 - 3.55 (m, 2H), 2.41 (s, 2H), 1.31 - 1.24 (m, 9H)

Example 264:

(6S)-3-[(3R)-3-hydroxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

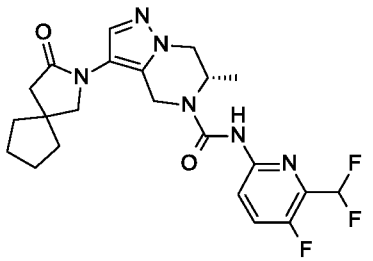


Preparation of (6S)-3-[(3R)-3-hydroxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 264)

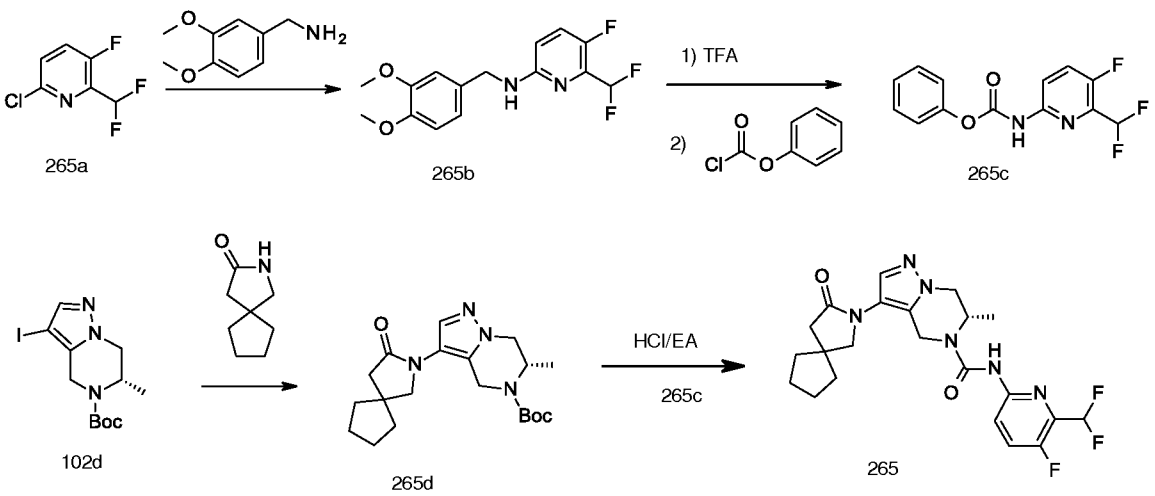
The title compound was prepared in analogy to Example **223** by using (3R)-3-hydroxypyrrolidin-2-one instead of pyrrolidin-2-one and phenyl N-(3,4,5-trifluorophenyl)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 264** was obtained as a solid (13 mg). LCMS ($M+H^+$): 410. ^{1}H NMR (400MHz, MeOD) δ ppm 7.65 (s, 1H), 7.34-7.27 (m, 2H), 5.10 (d, *J*=17.1 Hz, 1H), 4.98 - 4.95 (m, 1H), 4.54 - 4.42 (m, 2H), 4.30 (dd, *J*=4.4, 12.9 Hz, 1H), 4.16 (dd, *J*=1.3, 12.8 Hz, 1H), 3.78 (dd, *J*=4.8, 8.8 Hz, 2H), 2.64 - 2.52 (m, 1H), 2.16 - 2.01 (m, 1H), 1.26 (d, *J*=7.0 Hz, 3H)

Example 265:

(6S)-N-[6-(difluoromethyl)-5-fluoro-2-pyridyl]-6-methyl-3-(3-oxo-2-azaspiro[4.4]nonan-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of 6-(difluoromethyl)-N-(3,4-dimethoxybenzyl)-5-fluoropyridin-2-amine (compound 265b)

To a mixture of 3,4-dimethoxybenzylamine (752 mg, 4.5 mmol) and 6-chloro-2-(difluoromethyl)-3-fluoropyridine (545 mg, 3.0 mmol) in dioxane (15.0 mL) was added cesium carbonate (1.95 g, 6 mmol), tris(dibenzylideneacetone)dipalladium (137 mg, 0.15 mmol) and 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (174 mg, 0.30 mmol). The reaction mixture was flushed with nitrogen and refluxed for 5 hours. The reaction mixture was cooled down, diluted with EtOAc, and washed with ice-water. The organic phase was separated and concentrated. The residue was purified by silica gel column to give compound **265b** (375 mg). LCMS ($M+H^+$): 313.

Preparation of phenyl (6-(difluoromethyl)-5-fluoropyridin-2-yl)carbamate (compound 265c)

The reaction mixture of compound 6-(difluoromethyl)-N-(3,4-dimethoxybenzyl)-5-fluoropyridin-2-amine (compound **265b**, 312 mg, 1.0 mmol) and trifluoroacetic acid (3.0 mL) was stirred under reflux overnight in a sealed tube. The reaction mixture was cooled and concentrated. The residue was dissolved in DCM (3.0 mL), to which was added DIPEA (1.0 mL, 5.83 mmol) and phenyl chloroformate (235 mg, 1.5 mmol). The reaction mixture was stirred at 40 °C for 3 hours. The reaction mixture was concentrated and the residue was purified by silica gel column to give compound **265c** (141 mg). LCMS ($M+H^+$): 283.

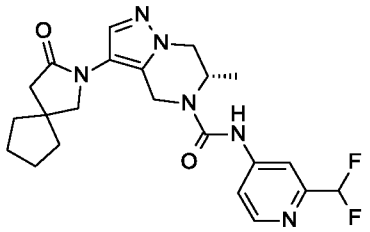
Preparation of (6S)-N-[6-(difluoromethyl)-5-fluoro-2-pyridyl]-6-methyl-3-(3-oxo-2-azaspiro[4.4]nonan-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 265)

The title compound was prepared in analogy to Example **223** by using 2-azaspiro[4.4]nonan-3-one instead of pyrrolidin-2-one and phenyl (6-(difluoromethyl)-5-

fluoropyridin-2-yl)carbamate (compound **265c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 265** was obtained as a white solid (15 mg). LCMS ($M+H^+$): 463. ^1H NMR (400MHz, MeOD) δ ppm 8.04 (dd, *J*=3.4, 9.2 Hz, 1H), 7.71 (t, *J*=9.3 Hz, 1H), 7.63 (s, 1H), 6.83 (t, *J*=56 Hz, 1H), 5.09 (d, *J*=16.8 Hz, 1H), 5.03 - 4.96 (m, 1H), 4.54 (d, *J*=16.8 Hz, 1H), 4.32 (dd, *J*=4.3, 12.5 Hz, 1H), 4.21 - 4.12 (m, 1H), 3.80 - 3.63 (m, 2H), 2.53 (s, 2H), 1.79 (s, 8H), 1.29 (d, *J*=6.8 Hz, 3H)

Example 266:

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-6-methyl-3-(3-oxo-2-azaspiro[4.4]nonan-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

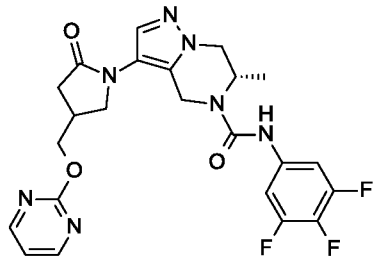


Preparation of (6S)-N-[2-(difluoromethyl)-4-pyridyl]-6-methyl-3-(3-oxo-2-azaspiro[4.4]nonan-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 266)

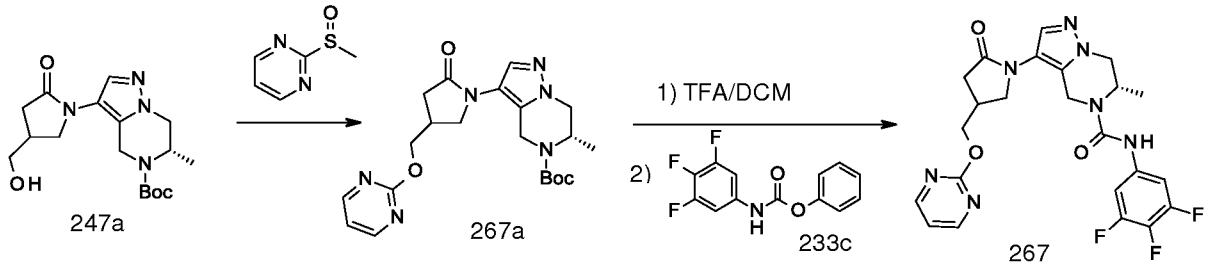
The title compound was prepared in analogy to Example **223** by using 2-azaspiro[4.4]nonan-3-one instead of pyrrolidin-2-one. **Example 266** was obtained as a white solid (44 mg). LCMS ($M+H^+$): 445. ^1H NMR (400MHz, MeOD) δ ppm 8.42 (d, *J*=5.5 Hz, 1H), 7.87 (d, *J*=2.0 Hz, 1H), 7.68 (dd, *J*=2.3, 5.8 Hz, 1H), 7.62 (s, 1H), 6.67 (t, *J*=56 Hz, 1H), 5.10 (d, *J*=17.1 Hz, 1H), 5.04 - 4.95 (m, 1H), 4.55 (d, *J*=16.8 Hz, 1H), 4.32 (dd, *J*=4.5, 12.8 Hz, 1H), 4.17 (dd, *J*=1.1, 12.7 Hz, 1H), 3.77 - 3.67 (m, 2H), 2.53 (s, 2H), 1.79 (s, 8H), 1.30 (d, *J*=6.8 Hz, 3H).

Example 267:

(6S)-6-methyl-3-[2-oxo-4-(pyrimidin-2-yloxymethyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: preparation of (6S)-tert-butyl 6-methyl-3-(2-oxo-4-((pyrimidin-2-yloxy)methyl)pyrrolidin-1-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 267a)

A 10 mL vial was charged with (6S)-tert-butyl 3-(4-(hydroxymethyl)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **247a**, 105 mg, 300 μmol,), 2-(methylsulfinyl)pyrimidine (63.9 mg, 449 μmol), potassium carbonate (82.8 mg, 599 μmol) and dioxane (5 mL). The vial was sealed and heated at 80 °C for 16 hours. The reaction mixture was poured into 20 mL of H_2O and extracted with EtOAc twice. The organic layers were combined, washed with brine (50 mL) and then concentrated to give crude compound **267a** as a light yellow oil (100 mg). LCMS ($M+H^+$): 429

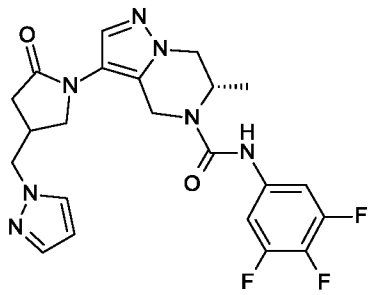
Step 2: preparation pf (6S)-6-methyl-3-[2-oxo-4-(pyrimidin-2-yloxymethyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 267)

A solution of (6S)-tert-butyl 6-methyl-3-(2-oxo-4-((pyrimidin-2-yloxy)methyl)pyrrolidin-1-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **267a**, 100 mg, 233 μmol) in 2,2,2-trifluoroacetic acid (4.96 g, 43.5 mmol) and DCM (5 mL) was stirred at room temperature for 30 mins. The reaction mixture was concentrated, the residue was dissolved in DMF (5 mL), to which then was added N-ethyl-N-isopropylpropan-2-amine (151 mg, 1.17 mmol) and phenyl (3,4,5-trifluorophenyl)carbamate (74.8 mg, 280 μmol). The reaction mixture was stirred at 70 °C for 0.5 hour. The reaction mixture was diluted with ethyl acetate (30 mL), and washed with water. The combined organic layer was dried over Na_2SO_4, and concentrated under vacuum. The crude product was purified by prep-HPLC to give Example **267** as a white solid (58

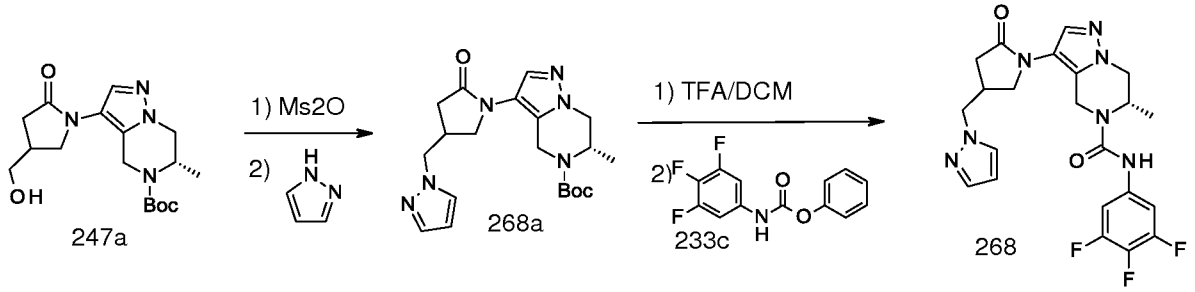
mg). LCMS (M+H$^+$): 502. ^{1}H NMR (400MHz, MeOD) δ ppm 8.59 (dd, *J*=3.4, 4.8 Hz, 2H), 7.65 (d, *J*=2.1 Hz, 1H), 7.31 - 7.27 (m, 2H), 7.14 (dt, *J*=1.5, 4.9 Hz, 1H), 5.12 - 5.02 (m, 1H), 5.01 - 4.95 (m, 1H), 4.61 - 4.49 (m, 3H), 4.30 (dd, *J*=4.2, 12.7 Hz, 1H), 4.20 - 4.05 (m, 2H), 3.90 - 3.80 (m, 1H), 3.15-3.11 (m, 1H), 2.86 - 2.79 (m, 1H), 2.59 - 2.53 m, 1H), 1.28-1.25 (m, 3H).

Example 268:

(6S)-6-methyl-3-[2-oxo-4-(pyrazol-1-ylmethyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: preparation of (6S)-tert-butyl 3-(4-((1H-pyrazol-1-yl)methyl)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 268a)

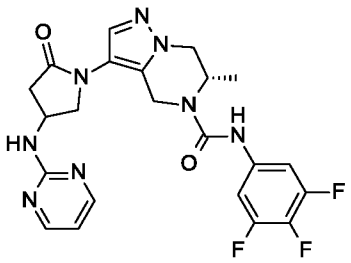
To a mixture of (6S)-tert-butyl 3-(4-(hydroxymethyl)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **247a**, 200 mg, 571 μmol) and DIPEA (221 mg, 1.71 mmol) in DCM (10 mL) was added methanesulfonic anhydride (199 mg, 1.14 mmol) slowly. After stirred at room temperature for 1 hour, the reaction mixture was poured into 50 mL of H_2O and extracted with DCM (50 mL). The organic layers were dried over Na_2SO_4 and concentrated in *vacuo* to give an oil. To a solution of the oil in acetonitrile (10 mL) was added 1H-pyrazole (47.7 mg, 700 μmol) and Cs_2CO_3 (342 mg, 1.05 mmol). The reaction mixture was heated to 80 °C for 2 hours. The reaction mixture was concentrated and the residue was purified by flash chromatography to give compound **268a** as a colorless oil. LCMS (M+H$^+$): 401.

Step 2: preparation of (6S)-6-methyl-3-[2-oxo-4-(pyrazol-1-ylmethyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 268)

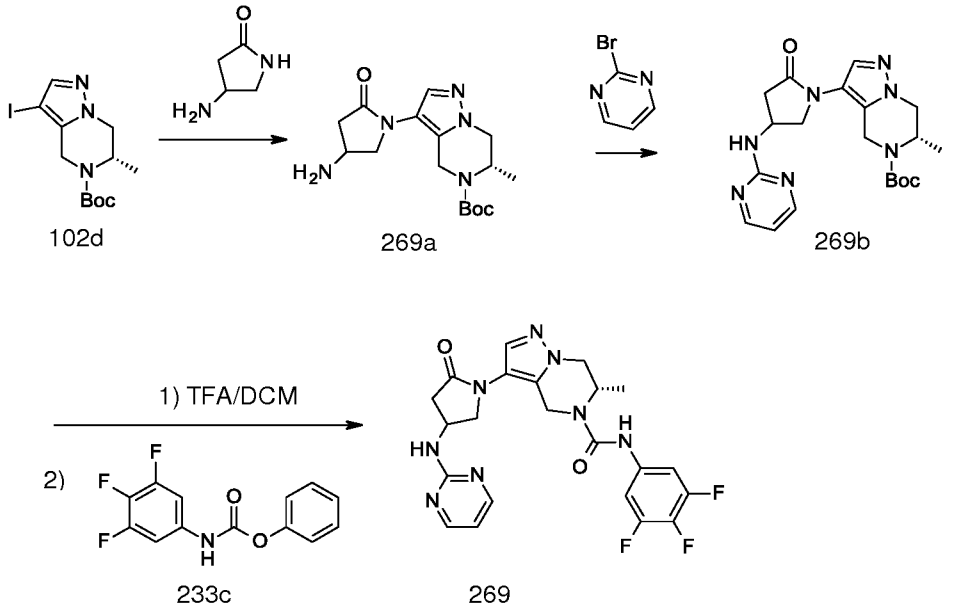
A solution of (6S)-tert-butyl 3-(4-((1H-pyrazol-1-yl)methyl)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **268a**, 100 mg, 250 μmol) in 2,2,2-trifluoroacetic acid (2 mL) and DCM (5 mL) was stirred at room temperature for 30 mins, and then concentrated. The residue was dissolved in DMF (5 mL), to which was added N-ethyl-N-isopropylpropan-2-amine (161 mg, 1.25 mmol) and phenyl (3,4,5-trifluorophenyl)carbamate (80.1 mg, 300 μmol). The reaction mixture was stirred at 70 °C for 0.5 hours. The reaction mixture was purified by prep-HPLC to give Example **268** as a white solid (60 mg). LCMS ($M+H^+$): 474. ^1H NMR (400MHz, MeOD) δ ppm 7.62 (d, *J*=2.1 Hz, 1H), 7.47 (s, 1H), 7.42 (d, *J*=1.5 Hz, 1H), 7.22-7.13 (m, 2H), 6.22 (t, *J*=2.1 Hz, 1H), 4.88 (d, *J*=16.9 Hz, 1H), 4.84 - 4.78 (m, 1H), 4.33 (d, *J*=16.9 Hz, 1H), 4.24 (d, *J*=7.0 Hz, 2H), 4.16 (dd, *J*=4.5, 12.8 Hz, 1H), 4.03 (dd, *J*=1.1, 12.7 Hz, 1H), 3.78 (dd, *J*=7.9, 10.0 Hz, 1H), 3.60 (dd, *J*=5.3, 10.0 Hz, 1H), 3.05 - 2.93 (m, 1H), 2.58 (dd, *J*=9.0, 17.4 Hz, 1H), 2.33 (dd, *J*=6.2, 17.4 Hz, 1H), 1.14 (d, *J*=6.8 Hz, 3H).

Example 269:

(6S)-6-methyl-3-[2-oxo-4-(pyrimidin-2-ylamino)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: preparation of (6S)-tert-butyl 3-(4-amino-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 269a)

A mixture of 4-aminopyrrolidin-2-one (276 mg, 2.75 mmol), (S)-tert-butyl 3-iodo-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (1 g, 2.75 mmol), potassium phosphate (877 mg, 4.13 mmol), copper(I) iodide (210 mg, 1.1 mmol) and (1R,2R)-N1,N2-dimethylcyclohexane-1,2-diamine (157 mg, 1.1 mmol) in DMSO (5 mL) was heated in microwave at 120 °C for 2 hours. The reaction mixture was diluted with water, and extracted with DCM/iPrOH (v/v=5:1, 30 mL) two times. The combined organic layer was dried over Na_2SO_4 and concentrated. The crude product was purified by flash chromatography (silica gel, 10% to 30% MeOH in DCM) to give compound **269a** as a colorless oil (500 mg). LCMS ($M+H^+$): 336.

Step 2: preparation of (6S)-tert-butyl 6-methyl-3-(2-oxo-4-(pyrimidin-2-ylamino)pyrrolidin-1-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 269b)

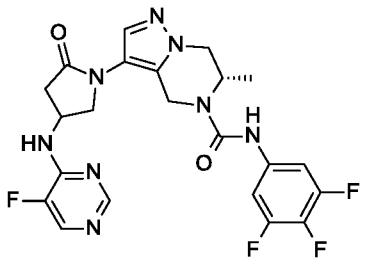
To a mixture of (6S)-tert-butyl 3-(4-amino-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **269a**, 339 mg, 1.01 mmol) in dry dioxane was added 2-bromopyrimidine (209 mg, 1.31 mmol) and DIPEA (392 mg, 3.03 mmol). The reaction mixture was heated under reflux overnight, and then concentrated. The obtained residue was then taken up in DCM, and washed with brine. The organic layer was separated, dried over Na_2SO_4 and concentrated in *vacuo* to afford crude compound **269b** as a yellow oil, which was directly used in next step without further purification. LCMS ($M+H^+$): 414.

Step 3: preparation of (6S)-6-methyl-3-[2-oxo-4-(pyrimidin-2-ylamino)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 269)

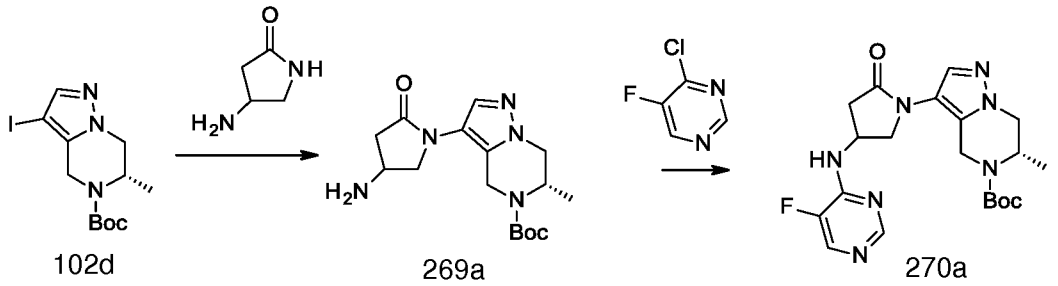
A solution of (6S)-tert-butyl 6-methyl-3-(2-oxo-4-(pyrimidin-2-ylamino)pyrrolidin-1-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **269b**, 418 mg, 1.01 mmol) in TFA (4 mL) and DCM (4 mL) was stirred at room temperature for 2 hours. The solvents were then removed and the residue was dissolved in DCM, to which was added phenyl (3,4,5-trifluorophenyl)carbamate (405 mg, 1.52 mmol) and DIPEA (1.31 g, 10.1 mmol). The reaction mixture was stirred at room temperature overnight. After concentration, the reaction mixture was purified by prep-HPLC purification to give **Example 269** as a white solid (40 mg). LCMS ($M+H^+$): 487. ^{1}H NMR (400MHz, MeOD) δ ppm 8.22 (d, *J*=4.8 Hz, 2H), 7.51 (d, *J*=1.3 Hz, 1H), 7.19 - 7.14 (m, 2H), 6.57 (t, *J*=4.6 Hz, 1H), 4.94 (dd, *J*=2.4, 17.0 Hz, 1H), 4.87 - 4.79 (m, 1H), 4.68 - 4.58 (m, 1H), 4.40 (dd, *J*=5.1, 17.0 Hz, 1H), 4.22 - 4.08 (m, 2H), 4.03 (dd, *J*=0.8, 12.8 Hz, 1H), 3.65 (dt, *J*=4.1, 9.9 Hz, 1H), 2.90 (dd, *J*=8.4, 17.1 Hz, 1H), 2.51 (dd, *J*=4.9, 17.4 Hz, 1H), 1.16 -1.13 (m, 3H).

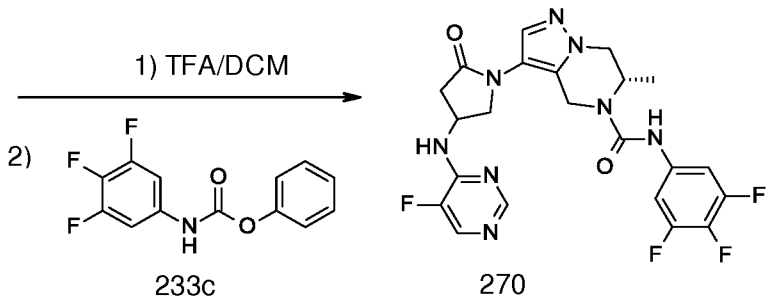
Example 270:

(6S)-3-[4-[(5-fluoropyrimidin-4-yl)amino]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



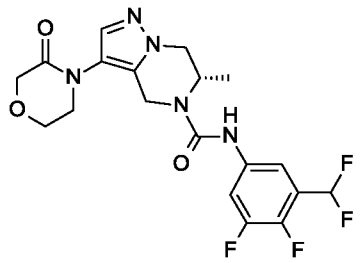


Preparation of Example 270

The title compound was prepared in analogy to Example **269** by using 4-chloro-5-fluoro-pyrimidine instead of 2-chloro-pyrimidine. **Example 270** was obtained as a solid (300 mg). LCMS ($M+H^+$): 505. ^1H NMR (400MHz, MeOD) δ ppm 8.42 - 8.31 (m, 1H), 8.23 - 8.02 (m, 1H), 7.65 (d, *J*=2.4 Hz, 1H), 7.33 - 7.24 (m, 2H), 5.07 (dd, *J*=1.9, 16.9 Hz, 1H), 4.98 - 4.93 (m, 2H), 4.52 (d, *J*=17.0 Hz, 1H), 4.36 - 4.24 (m, 2H), 4.19 - 4.12 (m, 1H), 3.89 - 3.77 (m, 1H), 3.06 (ddd, *J*=1.6, 8.6, 17.5 Hz, 1H), 2.77 - 2.66 (m, 1H), 1.32 - 1.23 (m, 3H).

Example 271:

(6S)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-6-methyl-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



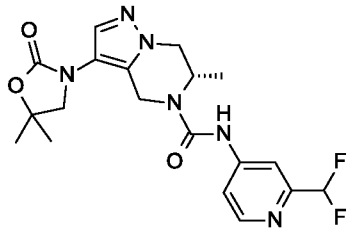
Preparation of (6S)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-6-methyl-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 271)

The title compound was prepared in analogy to Example **223** by using morpholin-3-one instead of pyrrolidin-2-one and phenyl N-[3-(difluoromethyl)-4,5-difluoro-phenyl]carbamate

(compound **239a**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 271** was obtained as a white solid (45 mg). LCMS ($M+H^+$): 442. ^1H NMR (400MHz, $CDCl_3$) δ ppm 7.83 (s, 1H), 7.72 - 7.68 (m, 1H), 7.52 (s, 1H), 7.38 (br. s., 1H), 6.86 (t, *J*=56 Hz, 1H), 5.14 - 5.04 (m, 1H), 4.90 (d, *J*=16.8 Hz, 1H), 4.39 (s, 2H), 4.36 - 4.25 (m, 2H), 4.16 - 4.01 (m, 3H), 4.00 - 3.91 (m, 1H), 3.76-3.70 (m, 1H), 1.40 (d, *J*=7.0 Hz, 3H).

Example 272:

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-3-(5,5-dimethyl-2-oxo-oxazolidin-3-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

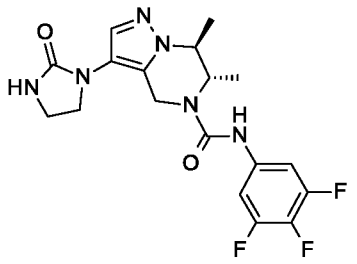


Preparation of (6S)-N-[2-(difluoromethyl)-4-pyridyl]-3-(5,5-dimethyl-2-oxo-oxazolidin-3-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 272)

The title compound was prepared in analogy to Example **223** by using 5,5-dimethyloxazolidin-2-one instead of pyrrolidin-2-one. Example **272** was obtained as a white solid (35 mg). LCMS ($M+H^+$): 421. ^1H NMR (400MHz, $CDCl_3$) δ ppm 8.88 (br. s., 1H), 8.45 (br. s., 1H), 8.01 (br. s., 1H), 7.83 (br. s., 1H), 7.44 (s, 1H), 6.72 (t, *J*=55 Hz, 1H), 5.27 (d, *J*=16.8 Hz, 1H), 5.14 (br. s., 1H), 4.55 (d, *J*=16.6 Hz, 1H), 4.33 (d, *J*=9.3 Hz, 1H), 4.09 (d, *J*=12.3 Hz, 1H), 3.82 (d, *J*=8.3 Hz, 1H), 3.73 (d, *J*=8.5 Hz, 1H), 1.61 (d, *J*=4.5 Hz, 6H), 1.36 (d, *J*=6.5 Hz, 3H)

Example 273:

(6S,7S)-6,7-dimethyl-3-(2-oxoimidazolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

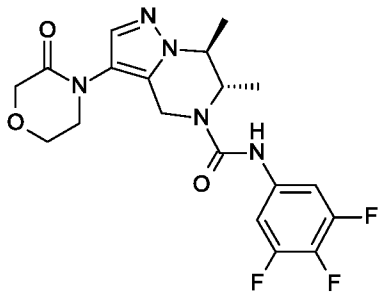


Preparation of (6S,7S)-6,7-dimethyl-3-(2-oxoimidazolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 273)

The title compound was prepared in analogy to Example **251** by using imidazolidin-2-one instead of pyrrolidin-2-one. **Example 273** was obtained as a white solid (30 mg). LCMS ($M+H^+$): 409. ^1H NMR (400MHz, $CDCl_3$) δ ppm 7.84 (br. s., 1H), 7.41 (s, 1H), 7.27-7.20 (m, 2H), 5.11 (d, *J*=16.6 Hz, 1H), 4.84 - 4.76 (m, 1H), 4.43 (d, *J*=16.6 Hz, 1H), 4.31 - 4.20 (m, 1H), 4.00 (q, *J*=8.6 Hz, 1H), 3.91 - 3.79 (m, 1H), 3.66 (t, *J*=8.0 Hz, 2H), 1.47 (d, *J*=6.5 Hz, 3H), 1.30 (d, *J*=6.8 Hz, 3H)

Example 274:

(6S,7S)-6,7-dimethyl-3-(3-oxomorpholin-4-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

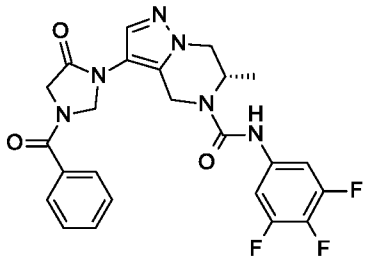


Preparation of (6S,7S)-6,7-dimethyl-3-(3-oxomorpholin-4-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 274)

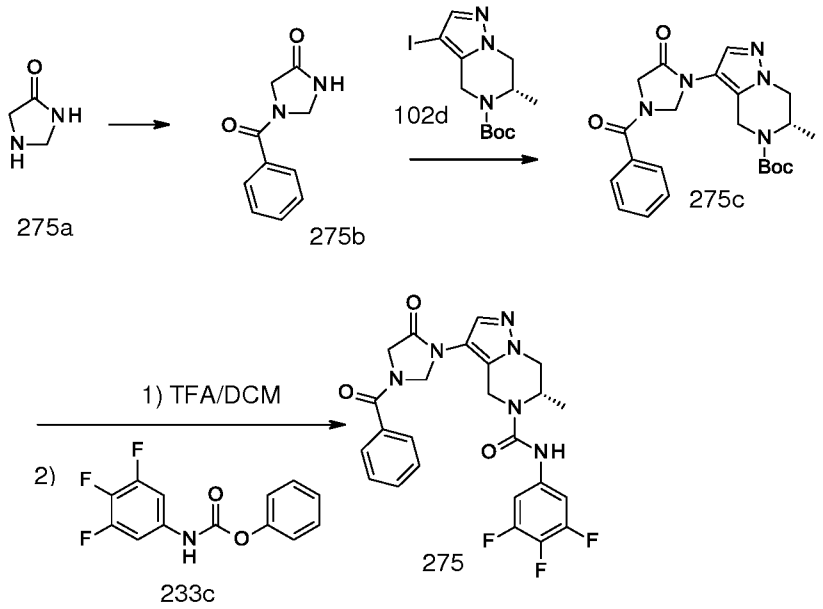
The title compound was prepared in analogy to Example **251** by using morpholin-3-one instead of pyrrolidin-2-one. **Example 274** was obtained as a white solid (23 mg). LCMS ($M+H^+$): 424. ^1H NMR (400MHz, $CDCl_3$) δ ppm 7.53 (s, 1H), 7.45 (s, 1H), 7.29-7.22 (m, 2H), 4.88 (d, *J*=16.3 Hz, 1H), 4.84 - 4.77 (m, 1H), 4.38 (s, 2H), 4.36 - 4.27 (m, 2H), 4.15 - 4.01 (m, 2H), 3.99 - 3.88 (m, 1H), 3.77 - 3.72 (m, 1H), 1.49 (d, *J*=6.8 Hz, 3H), 1.31 (d, *J*=7.0 Hz, 3H)

Example 275:

(6S)-3-(3-benzoyl-5-oxo-imidazolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of 1-benzoylimidazolidin-4-one (compound 275b)

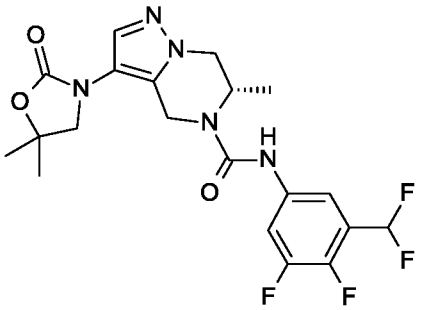
To a suspension of imidazolidin-4-one (861 mg, 10 mmol) and K_2CO_3 (5.53 g, 40 mmol) in THF (30 mL) was added slowly benzoyl chloride (1.41 g, 10 mmol). Then the reaction mixture was stirred at room temperature for 15 hours. Then the solid was filtered and the filtrate was concentrated to give crude compound **275b** as a light yellow solid (1.5 g). LCMS ($M+H^+$): 191.

Preparation of (6S)-3-(3-benzoyl-5-oxo-imidazolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 275)

The title compound was prepared in analogy to Example **262** by using 1-benzoylimidazolidin-4-one (compound **275b**) instead of (S)-3-hydroxypyrrolidin-2-one. **Example 275** was obtained as a white solid (36 mg). LCMS ($M+H^+$): 499. ^1H NMR (400MHz, MeOD) δ ppm 7.77 (br. s., 1H), 7.65 - 7.62(m, 2H), 7.60 - 7.51 (m, 3H), 7.32-7.26 (m, 2H), 5.43 (d, *J*=9.3 Hz, 1H), 5.35 - 5.23 (m, 1H), 5.16 - 5.01 (m, 1H), 4.96 (br. s., 1H), 4.58 - 4.45 (m, 1H), 4.43 - 4.25 (m, 3H), 4.23 - 4.13 (m, 1H), 1.30-1.26 m, 3H).

Example 276:

(6S)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-3-(5,5-dimethyl-2-oxo-oxazolidin-3-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

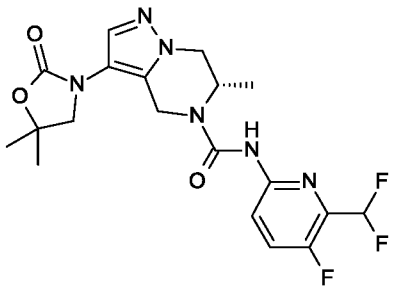


Preparation of (6S)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-3-(5,5-dimethyl-2-oxo-oxazolidin-3-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 276)

The title compound was prepared in analogy to Example **223** by using 5,5-dimethyloxazolidin-2-one instead of pyrrolidin-2-one and phenyl N-[3-(difluoromethyl)-4,5-difluoro-phenyl]carbamate (compound **239a**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 276** was obtained as a white solid (28 mg). LCMS ($M+H^+$): 456. ^{1}H NMR (400MHz, MeOD) δ ppm 7.78 - 7.60 (m, 2H), 7.46 (d, *J*=2.3 Hz, 1H), 7.01 (t, *J*=56 Hz, 1H), 5.09 (d, *J*=16.8 Hz, 1H), 5.03 - 4.95 (m, 1H), 4.56 (d, *J*=16.8 Hz, 1H), 4.37 - 4.25 (m, 1H), 4.17 (dd, *J*=1.0, 12.8 Hz, 1H), 3.91 - 3.76 (m, 2H), 1.58 (s, 6H), 1.27 (d, *J*=6.8 Hz, 3H).

Example 277:

(6S)-N-[6-(difluoromethyl)-5-fluoro-2-pyridyl]-3-(5,5-dimethyl-2-oxo-oxazolidin-3-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

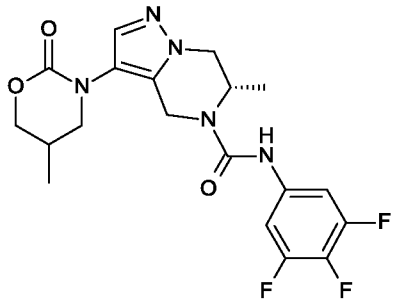


Preparation of (6S)-N-[6-(difluoromethyl)-5-fluoro-2-pyridyl]-3-(5,5-dimethyl-2-oxo-oxazolidin-3-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 277)

The title compound was prepared in analogy to Example **223** by using 5,5-dimethyloxazolidin-2-one instead of pyrrolidin-2-one and phenyl phenyl N-[6-(difluoromethyl)-5-fluoro-2-pyridyl]carbamate (compound **265b**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 277** was obtained as a white solid (10 mg). LCMS ($M+H^+$): 439. ^1H NMR (400MHz, MeOD) δ ppm 8.06 (dd, *J*=3.3, 9.3 Hz, 1H), 7.71 (t, *J*=9.3 Hz, 1H), 7.65 (s, 1H), 6.84 (t, *J*=56 Hz, 1H), 5.14 (d, *J*=17.1 Hz, 1H), 5.06 - 4.98 (m, 1H), 4.58 (d, *J*=17.1 Hz, 1H), 4.32 (dd, *J*=4.6, 12.9 Hz, 1H), 4.22 - 4.13 (m, 1H), 3.83 (q, *J*=8.7 Hz, 2H), 1.59 (s, 6H), 1.28 (d, *J*=6.8 Hz, 3H).

Example 278:

(6S)-6-methyl-3-(5-methyl-2-oxo-1,3-oxazinan-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

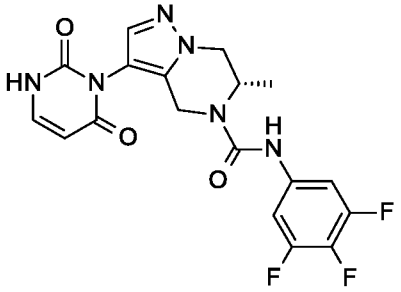


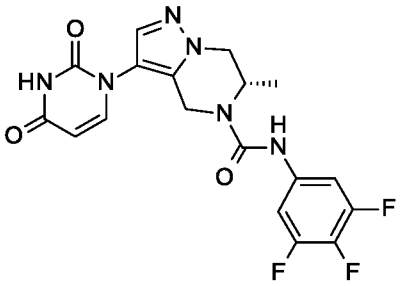
Preparation of (6S)-6-methyl-3-(5-methyl-2-oxo-1,3-oxazinan-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 278)

The title compound was prepared in analogy to Example **223** by using 5-methyl-1,3-oxazinan-2-one instead of pyrrolidin-2-one and phenyl N-(3,4,5-trifluoro-phenyl)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 278** was obtained as a white solid (70 mg). LCMS ($M+H^+$): 424. ^1H NMR (400MHz, MeOD) δ ppm 7.52 (s, 1H), 7.23 - 7.13 (m, 2H), 4.84 (dd, *J*=6.1, 16.8 Hz, 2H), 4.37 - 4.25 (m, 2H), 4.23 - 4.14 (m, 1H), 4.09 - 3.97 (m, 2H), 3.68 - 3.54 (m, 1H), 3.34 (ddd, *J*=9.3, 11.4, 15.1 Hz, 1H), 2.37 - 2.33 (m, 1H), 1.15 (dd, *J*=2.1, 6.9 Hz, 3H), 1.01 (d, *J*=6.7 Hz, 3H)

Example 279 and Example 280:

(6S)-3-(2,4-dioxo-1H-pyrimidin-3-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide and **(6S)-3-(2,4-dioxopyrimidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide**





Preparation of (6S)-3-(2,4-dioxo-1H-pyrimidin-3-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide and **(6S)-3-(2,4-dioxopyrimidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide**

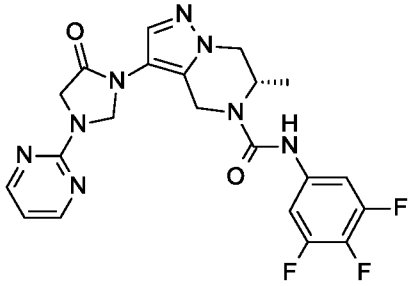
The title compounds were prepared in analogy to Example **223** by using 1H-pyrimidine-2,4-dione instead of pyrrolidin-2-one and phenyl N-(3,4,5-trifluoro-phenyl)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**).

Example 279 was obtained as a white solid (5 mg). LCMS ($M+H^+$): 421. ^1H NMR (400MHz, MeOD) δ ppm 7.59 (s, 1H), 7.52 (d, *J*=7.7 Hz, 1H), 7.31-7.23 (dd, *J*=6.4, 10.3 Hz, 2H), 5.83 (d, *J*=7.7 Hz, 1H), 5.06 - 4.98 (m, 1H), 4.91 - 4.84 (m, 1H), 4.41 - 4.29 (m, 2H), 4.20 (d, *J*=12.6 Hz, 1H), 1.29 (d, *J*=6.8 Hz, 3H)

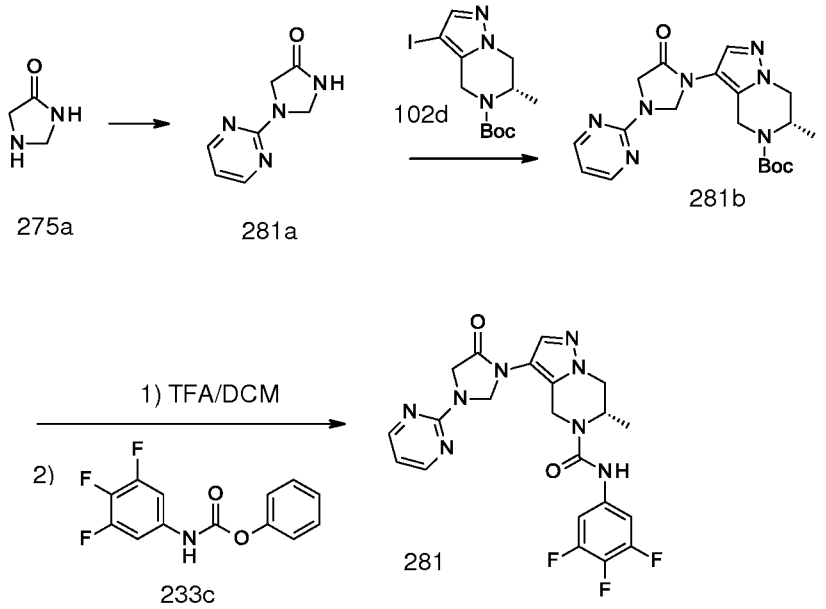
Examole 280 was obtained as a white solid (5 mg). LCMS ($M+H^+$): 421. ^1H NMR (400MHz, MeOD) δ ppm 7.71 (s, 1H), 7.66 (d, *J*=7.9 Hz, 1H), 7.32-7.24 (dd, *J*=6.4, 10.3 Hz, 2H), 5.81 (d, *J*=7.8 Hz, 1H), 5.06 - 4.97 (m, 2H), 4.47 (d, *J*=17.0 Hz, 1H), 4.39 - 4.30 (m, 1H), 4.26 - 4.17 (m, 1H), 1.29 (d, *J*=6.8 Hz, 3H)

Example 281:

(6S)-6-methyl-3-(5-oxo-3-pyrimidin-2-yl-imidazolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of 1-(pyrimidin-2-yl)imidazolidin-4-one (compound 281a)

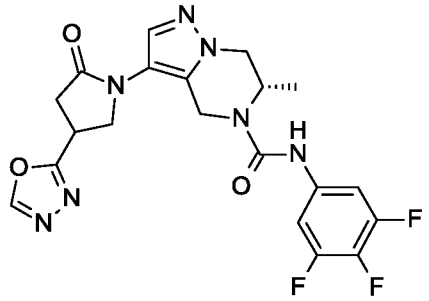
A mixture of imidazolidin-4-one hydrochloride (500 mg, 4.08 mmol), 2-bromopyrimidine (973 mg, 6.12 mmol) and potassium carbonate (1.69 g, 12.2 mmol) in dioxane (15 mL) were heated at 80 °C for 2 hours. The reaction mixture was filtered and the filtrate was concentrated. The crude product was purified by flash chromatography (silica gel, 10% to 20% MeOH in DCM) to give compound **281a** as a white solid (50 mg). LCMS ($M+H^+$): 165.

Preparation of (6S)-6-methyl-3-(5-oxo-3-pyrimidin-2-yl-imidazolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 281)

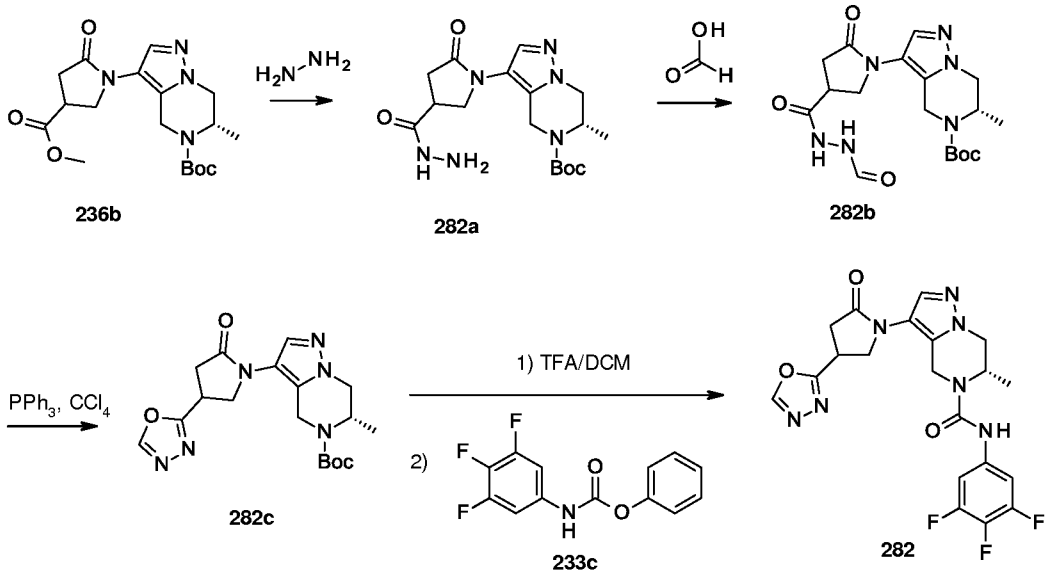
The title compound was prepared in analogy to Example **262** by using 1-(pyrimidin-2-yl)imidazolidin-4-one (compound **281a**) instead of (S)-3-hydroxypyrrolidin-2-one. **Example 281** was obtained as a white solid (30 mg). LCMS ($M+H^+$): 499. ^{1}H NMR (400MHz, MeOD) δ ppm 8.47 (d, *J*=4.9 Hz, 2H), 7.77 (s, 1H), 7.32-7.27 (m, 2H), 6.83 (t, *J*=4.9 Hz, 1H), 5.44 - 5.31 (m, 2H), 5.12 (d, *J*=16.9 Hz, 1H), 5.03 - 4.96 (m, 1H), 4.58 (d, *J*=16.9 Hz, 1H), 4.38 - 4.29 (m, 3H), 4.25 - 4.15 (m, 1H), 1.30 (d, *J*=6.8 Hz, 3H)

Example 282:

(6S)-6-methyl-3-[4-(1,3,4-oxadiazol-2-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: Preparation of (6S)-tert-butyl 3-(4-(hydrazinecarbonyl)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 282a)

A mixture of (6S)-tert-butyl 3-(4-(methoxycarbonyl)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (1.0 g, 2.64 mmol) and hydrazine hydrate (1.32 g, 26.4 mmol) in EtOH (20 mL) was stirred at 85 °C for 15 hours. The reaction mixture was concentrated in *vacuo* to give crude compound **282a** as a white solid (0.9 g). LCMS ($M+H^+$): 379.

Step 2: Preparation of (6S)-tert-butyl 3-(4-(2-formylhydrazinecarbonyl)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 282b)

A mixture of (6S)-tert-butyl 3-(4-(hydrazinecarbonyl)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **282a**, 500 mg, 1.32 mmol) and HCOOH (2 mL) in DCM (10 mL)was stirred at 50 °C for 2 hours. The reaction mixture was then concentrated in *vacuo* to give crude compound **282b** as a white solid (0.55 g). LCMS ($M+H^+$): 407.

Step 3: Preparation of (6S)-tert-butyl 3-(4-(1,3,4-oxadiazol-2-yl)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 282c)

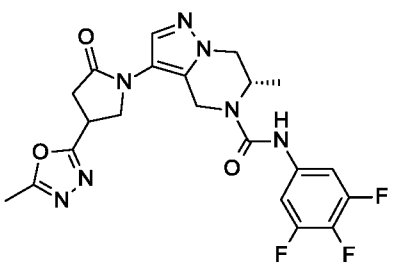
A mixture of (6S)-tert-butyl 3-(4-(2-formylhydrazinecarbonyl)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **282b**, 500 mg, 1.23 mmol), triphenylphosphine (1.94 g, 7.38 mmol), triethylamine (622 mg, 6.15 mmol) and CCl_4 (1.89 g, 12.3 mmol) in acetonitrile (12 mL) was stirred at room temperature for 1 hour. The reaction mixture was diluted with EtOAc (50 mL), and washed with saturated aqueous $NaHCO_3$ solution (20 mL) and brine (20 mL). The organic layer was dried over Na_2SO_4 and concentrated in *vacuo*. The crude product was purified by flash chromatography (silica gel, 10% MeOH in EtOAc) to give compound **282c** as a colorless oil (0.3 g). LCMS ($M+H^+$): 389.

Step 4: Preparation of (6S)-6-methyl-3-[4-(1,3,4-oxadiazol-2-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 282)

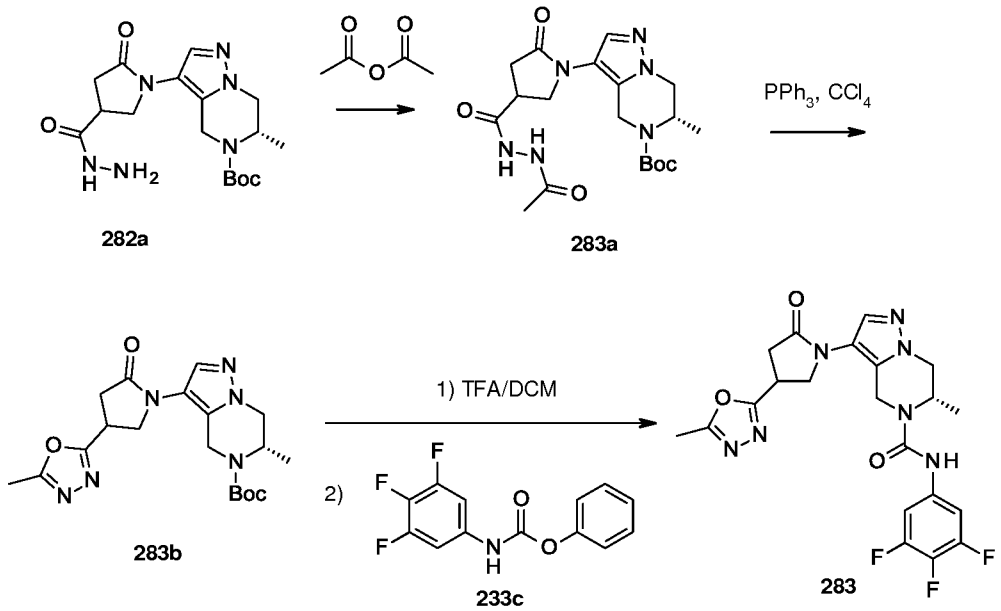
A solution of (6S)-tert-butyl 3-(4-(1,3,4-oxadiazol-2-yl)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **282c**, 300 mg, 0.77 mmol) in 2,2,2-trifluoroacetic acid (5 mL) and DCM (10 mL) was stirred at room temperature for 30 mins. The reaction mixture was concentrated and the residue was dissolved in DMF (5 mL), then to which were added N-ethyl-N-isopropylpropan-2-amine (499 mg, 3.86 mmol), and phenyl (3,4,5-trifluorophenyl)carbamate (248 mg, 0.92 mmol). The reaction mixture was stirred at 70 °C for 0.5 hours. The reaction mixture was purified by prep-HPLC to give **Example 282** as a white solid (90 mg). LCMS ($M+H^+$): 462. ^1H NMR (400MHz, MeOD) δ ppm 8.99 (s, 0.5H), 8.98 (s, 0.5H) 7.68 (s, 0.5H), 7.67 (s, 0.5H), 7.32-7.27 (m, 2H), 5.05 (dd, *J*=12.2, 16.9 Hz, 1H), 4.99 - 4.92 (m, 1H), 4.51 (dd, *J*=8.0, 16.8 Hz, 1H), 4.40 - 4.26 (m, 2H), 4.25 - 4.10 (m, 3H), 3.18 - 3.07 (m, 1H), 3.04 - 2.92 (m, 1H), 1.29 - 1.26 (m, 3H).

Example 283:

(6S)-6-methyl-3-[4-(5-methyl-1,3,4-oxadiazol-2-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of tert-butyl (6S)-3-[4-(acetamidocarbamoyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 283a)

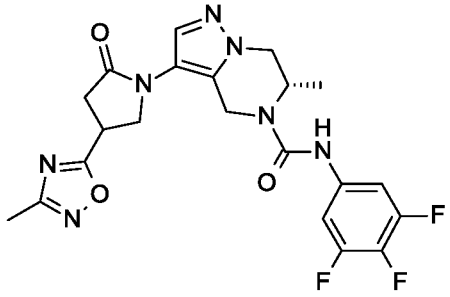
A mixture of acetic anhydride (162 mg, 1.59 mmol) and (6S)-tert-butyl 3-(4-(hydrazinecarbonyl)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **282a**, 300 mg, 793 μmol) in DCM (10 mL) was stirred at room temperature for 2 hours. The reaction mixture was concentrated in *vacuo* to give compound **283a** as a white solid (350 mg). LCMS ($M+H^+$): 421

Preparation of (6S)-6-methyl-3-[4-(5-methyl-1,3,4-oxadiazol-2-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 283)

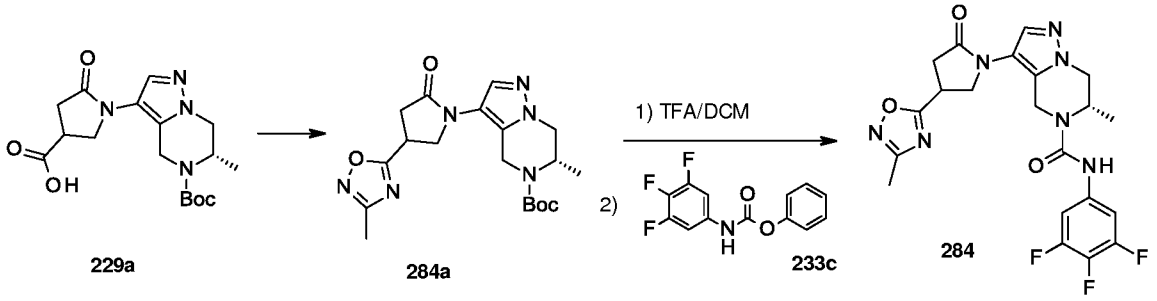
The title compound was prepared in analogy to Example **282** by using tert-butyl (6S)-3-[4-(acetamidocarbamoyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (**compound 283a**) instead of (6S)-tert-butyl 3-(4-(2-formylhydrazinecarbonyl)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate **(compound 282b)**. **Example 283** was obtained as a white solid (30 mg). LCMS ($M+H^+$): 476. ^{1}H NMR (400MHz, MeOD) δ ppm 7.66 (s, 1H), 7.32-7.27 (m, 2H), 5.10 - 4.93 (m, 2H), 4.51 (dd, *J*=7.3, 17.1 Hz, 1H), 4.35 - 4.25 (m, 2H), 4.20 - 4.09 (m, 3H), 3.16 - 3.02 (m, 1H), 3.00 - 2.90 (m, 1H), 2.57 (s, 1.5H), 2.56 (s, 1.5H), 1.29 - 1.26 (m, 3H).

Example 284:

(6S)-6-methyl-3-[4-(3-methyl-1,2,4-oxadiazol-5-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: Preparation of tert-butyl (6S)-6-methyl-3-[4-(3-methyl-1,2,4-oxadiazol-5-yl)-2-oxo-pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 284a)

A mixture of compound N'-hydroxyacetimidamide (915 mg, 12.3 mmol), 1-((S)-5-(tert-butoxycarbonyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)-5-oxopyrrolidine-3-carboxylic acid (compound **229a**, 3 g, 8.23 mmol), EDCI(2.37 g, 12.3 mmol), DIPEA (10.6 g, 82.3 mmol) and HOBt (334 mg, 2.47 mmol) in DCE (20 mL) was stirred at 80 °C for 16 hours. The reaction mixture was washed with water, the organic phase was dried and concentrated. The residue was purified by silica gel column to give compound **284a** as a light brown oil. LCMS ($M+H^+$): 403.

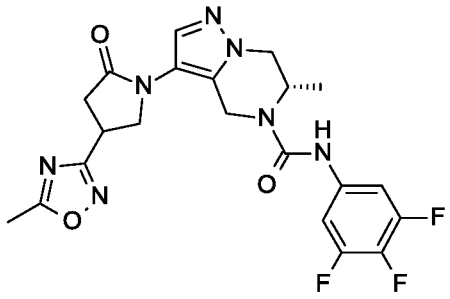
Step 2: preparation of (6S)-6-methyl-3-[4-(3-methyl-1,2,4-oxadiazol-5-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 284)

Removal of Boc protection in acidic conditions and condensation with phenyl (3,4,5-trifluorophenyl)carbamate were carried out in analogy to Example **282** to give Example **284** as white solid (15 mg). LCMS ($M+H^+$): 476. ^1H NMR (400MHz, MeOD) δ ppm 7.66 (s, 1H), 7.32-7.27 (m, 2H), 5.05 (dd, *J*=9.4, 16.9 Hz, 1H), 4.98 - 4.92 (m, 1H), 4.51 (dd, *J*=4.0, 17.1 Hz, 1H),

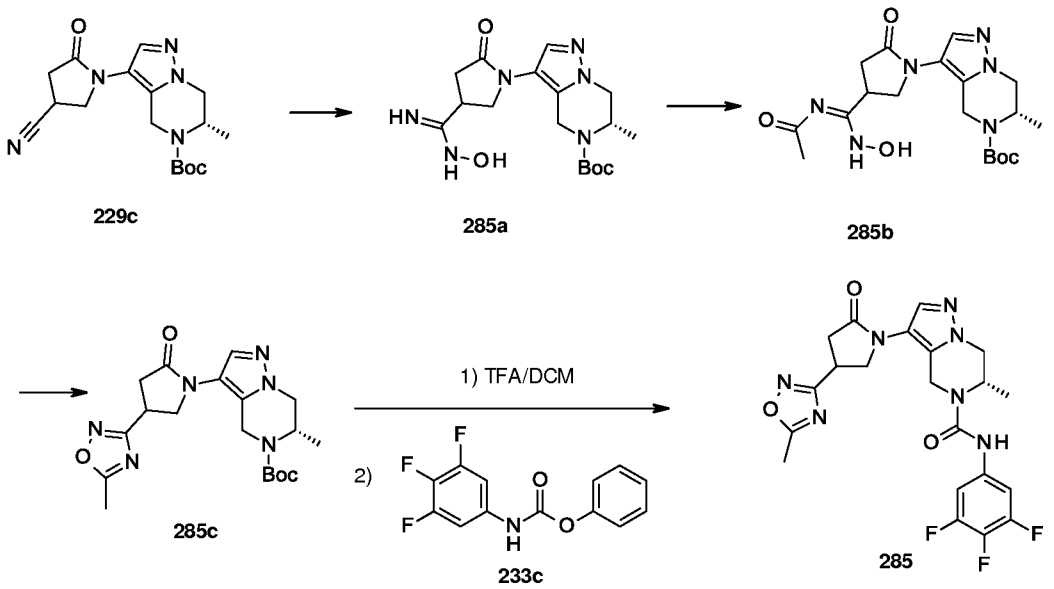
4.37 - 4.25 (m, 2H), 4.23 - 4.05 (m, 3H), 3.17 - 3.05 (m, 1H), 3.00 - 2.87 (m, 1H), 2.40 (s, 1.5H), 2.39 (s, 1.5H), 1.29 - 1.26 (m, 3H).

Example 285:

(6S)-6-methyl-3-[4-(5-methyl-1,2,4-oxadiazol-3-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: Preparation of (6S)-tert-butyl 3-(4-(N-hydroxycarbamimidoyl)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 285a)

A mixture of (6S)-tert-butyl 3-(4-cyano-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **229c**, 300 mg, 869 µmol), hydroxylamine hydrochloride (60.4 mg, 869 µmol) and DIPEA (112 mg, 152 µL, 869 µmol) in EtOH was stirred at 80 °C for 2 hours. The reaction mixture was concentrated in *vacuo* to give crude compound **285a** as a white solid (330 mg). LCMS ($M+H^+$): 379.

Step 2: Preparation of (6S)-tert-butyl 3-(4-N'-acetyl-N-hydroxycarbamimidoyl)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 285b)

A mixture of acetic anhydride (108 mg, 1.06 mmol) and (6S)-tert-butyl 3-(4-(N-hydroxycarbamimidoyl)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **285a**, 200 mg, 529 μmol) in DCM (10 mL) was stirred at room temperature for 1 hour. The reaction mixture was concentrated in *vacuo* to give compound **285b** as a colorless oil (200 mg). LCMS ($M+H^+$): 421.

Step 3: Preparation of (6S)-tert-butyl 6-methyl-3-(4-(5-methyl-1,2,4-oxadiazol-3-yl)-2-oxopyrrolidin-1-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 285c)

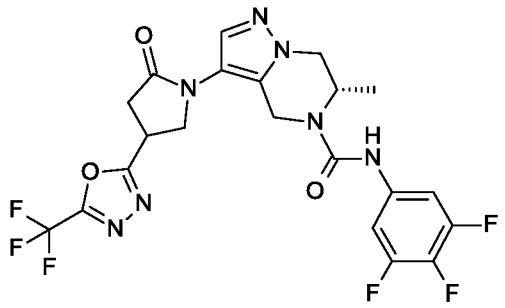
A mixture of (6S)-tert-butyl 3-(4-N'-acetyl-N-hydroxycarbamimidoyl)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **285b**, 200 mg, 476 μmol) and pyridine (5 mL) was stirred at 110 °C for 25 hours. The reaction mixture was concentrated in *vacuo* to give crude compound **285c** as a brown oil (200 mg). LCMS ($M+H^+$): 403.

Step 4: Preparation of (6S)-6-methyl-3-[4-(5-methyl-1,2,4-oxadiazol-3-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 285)

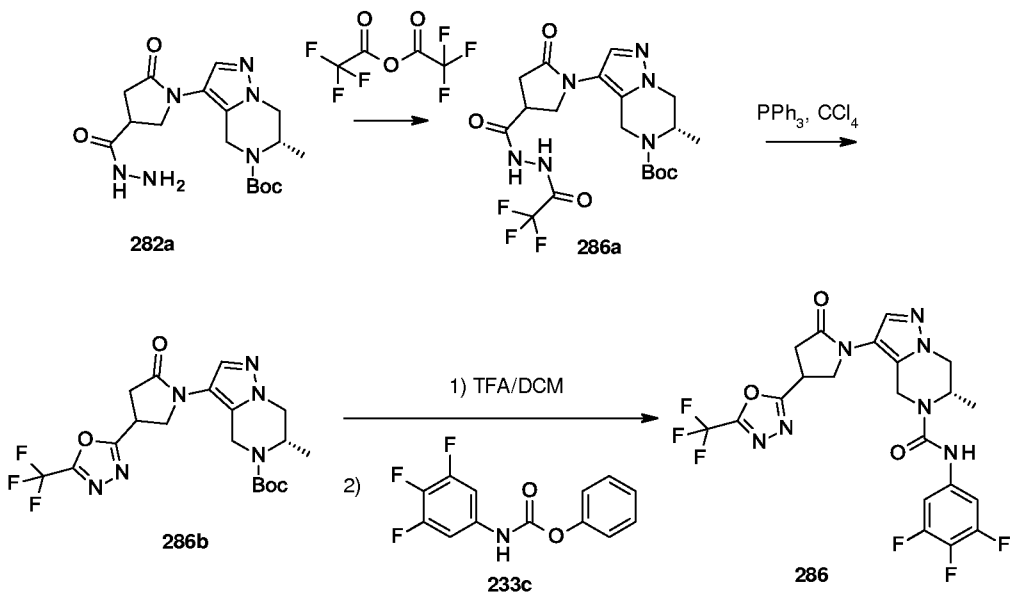
A solution of (6S)-tert-butyl 6-methyl-3-(4-(5-methyl-1,2,4-oxadiazol-3-yl)-2-oxopyrrolidin-1-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **285c**, 200 mg, 497 μmol) in 2,2,2-trifluoroacetic acid (3 mL) and DCM (6 mL) was stirred at room temperature for 30 mins. The reaction mixture was concentrated, and the resulting residue was dissolved in DMF (3 mL), to which then was added DIPEA (321 mg, 2.48 mmol), and phenyl (3,4,5-trifluorophenyl)carbamate (159 mg, 596 μmol). The reaction mixture was stirred at 70 °C for 0.5 hours, cooled down to room temperature, and then purified by prep-HPLC to give **Example 285** as white solid (120 mg). LCMS ($M+H^+$): 476. ^{1}H NMR (400MHz, MeOD) δ ppm 7.66 (s, 0.5H), 7.65 (s, 0.5H), 7.34 - 7.24 (m, 2H), 5.06 (dd, *J*=3.8, 17.1 Hz, 1H), 4.96 (d, *J*=6.3 Hz, 1H), 4.51 (d, *J*=17.1 Hz, 1H), 4.36 - 4.21 (m, 2H), 4.20 - 4.13 (m, 1H), 4.08 - 3.98 (m, 2H), 3.04 (dd, *J*=8.8, 16.6 Hz, 1H), 2.93 - 2.82 (m, 1H), 2.62 (d, *J*=2.8 Hz, 3H), 1.29-1.26 (m, 3H).

Example 286:

(6S)-6-methyl-3-[2-oxo-4-[5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl]pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of tert-butyl (6S)-6-methyl-3-[2-oxo-4-[[(2,2,2-trifluoroacetyl)amino]carbamoyl]pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 286a)

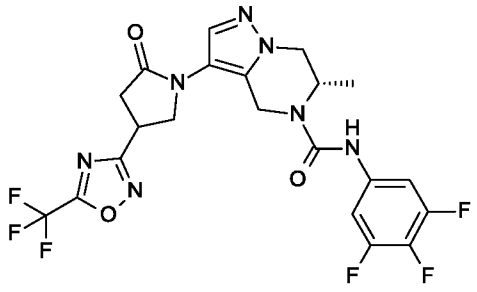
A mixture of 2,2,2-trifluoroacetic anhydride (167 mg, 793 µmol) and (6S)-tert-butyl 3-(4-(hydrazinecarbonyl)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **282a**, 150 mg, 396 µmol) in DCM (10 mL) was stirred at room temperature for 2 hours. The reaction mixture was concentrated in *vacuo* to give crude compound **286a** as a white solid (200 mg). LCMS ($M+H^+$): 475

Preparation of (6S)-6-methyl-3-[2-oxo-4-[5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl]pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 286)

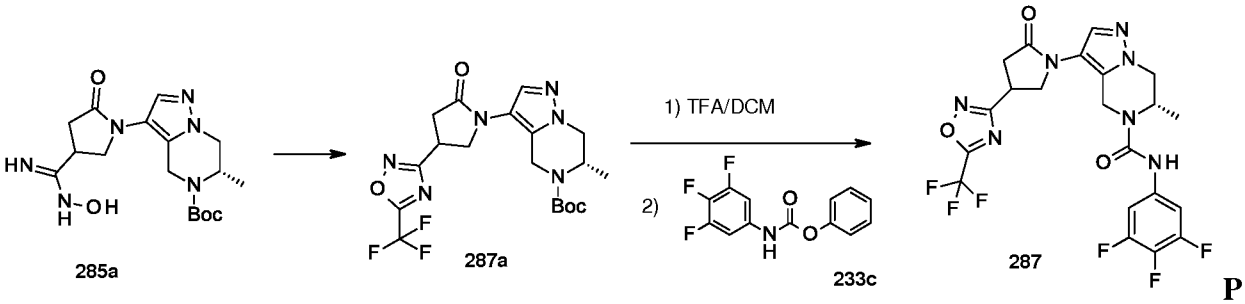
The title compound was prepared in analogy to **Example 282** by using tert-butyl (6S)-6-methyl-3-[2-oxo-4-[[(2,2,2-trifluoroacetyl)amino]carbamoyl]pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **286a**) instead of (6S)-tert-butyl 3-(4-(2-formylhydrazinecarbonyl)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **282b**). **Example 286** was obtained as a white solid (3 mg). LCMS ($M+H^+$): 530. ^1H NMR (400MHz, MeOD) δ ppm 7.69 (s, 0.5H), 7.65 (s, 0.5H), 7.32-7.27 (m, 2H), 5.12 - 5.00 (m, 1H), 4.99 - 4.92 (m, 1H), 4.56 - 4.46 (m, 1H), 4.37 - 4.22 (m, 4H), 4.20 - 4.13 (m, 1H), 3.19 - 3.10 (m, 1H), 3.09 - 2.99 (m, 1H), 1.28 (d, *J*=6.8 Hz, 3H).

Example 287:

(6S)-6-methyl-3-[2-oxo-4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



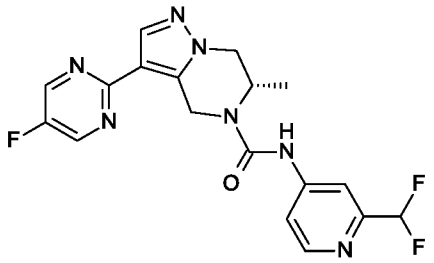
Preparation of (6S)-6-methyl-3-[2-oxo-4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 287)

The title compound was prepared in analogy to **Example 285** by using 2,2,2-trifluoroacetic anhydride instead of acetic anhydride. **Example 287** was obtained as a white solid (100 mg). LCMS ($M+H^+$): 530. ^1H NMR (400MHz, MeOD) δ ppm 7.69 (s, 0.5H), 7.65 (s, 0.5H), 7.33 - 7.24 (m, 2H), 5.06 (dd, *J*=12.4, 16.9 Hz, 1H), 5.00 - 4.94 (m, 1H), 4.52 (dd, *J*=4.5, 17.1 Hz, 1H),

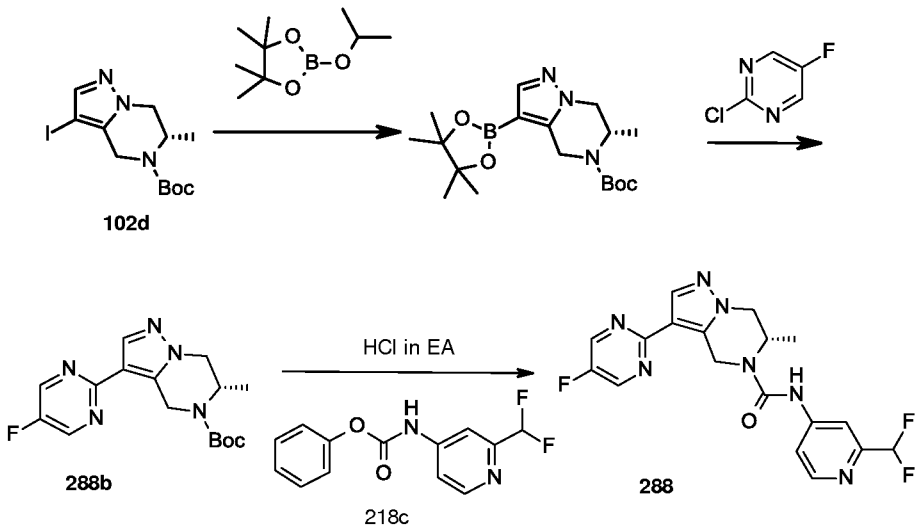
4.39 - 4.27 (m, 2H), 4.25 - 4.05 (m, 3H), 3.18 - 3.06 (m, 1H), 3.00 - 2.90 (m, 1H), 1.29-1.26 (m, 3H).

Example 288:

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-3-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of tert-butyl (6S)-3-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 288b):

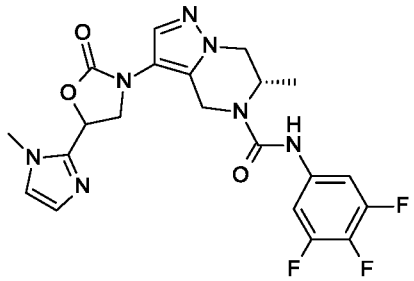
The compound **288b** was prepared in analogy to compound **67c** by using 2-chloro-5-fluoro-pyrimidine instead of 2-chloro-4-(trifluoromethyl)pyridine. Compound **288b** was obtained as a white solid (150 mg). LCMS ($M+H^+$): 334. ^1H NMR (400MHz, MeOD) δ ppm 8.72 (d, *J*=0.6 Hz, 2H), 8.18 (s, 1H), 5.40 (d, *J*=18.9 Hz, 1H), 4.89 (d, *J*=5.5 Hz, 1H), 4.65 (d, *J*=18.7 Hz, 1H), 4.34 - 4.25 (m, 1H), 4.22 - 4.12 (m, 1H), 1.55 (s, 9H), 1.23 (d, *J*=7.0 Hz, 3H).

Preparation of (6S)-N-[2-(difluoromethyl)-4-pyridyl]-3-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 288)

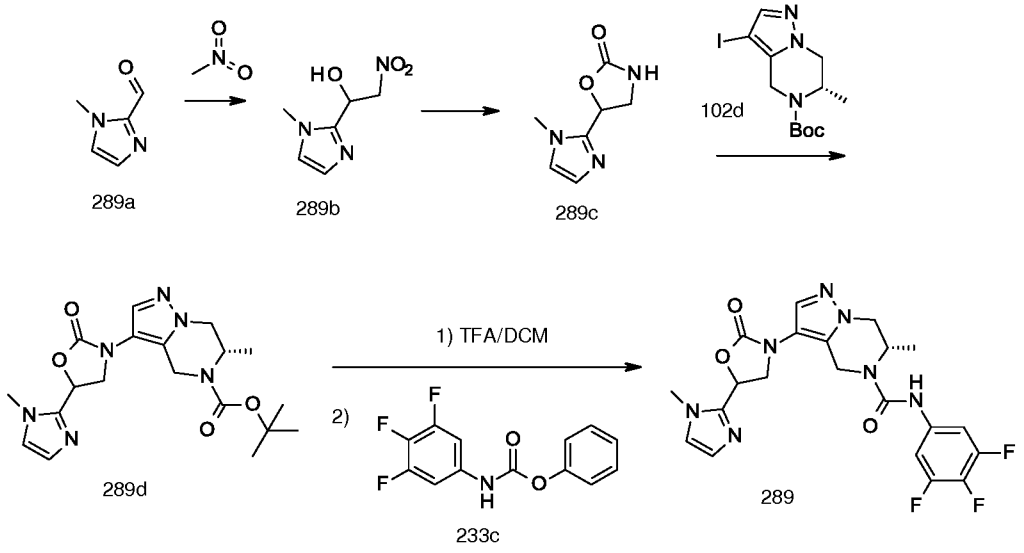
The title compound was prepared in analogy to **Example 223** by using tert-butyl (6S)-3-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **288b**) instead of tert-butyl (6S)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **223b**). **Example 288** was obtained as a white solid (6 mg). LCMS ($M+H^+$): 390. ^1H NMR (400MHz, $CDCl_3$) δ ppm 8.63 (s, 2H), 8.55 (d, *J*=6.3 Hz, 1H), 8.26 (s, 1H), 7.68 (d, *J*=2.5 Hz, 2H), 6.94 (s, 1H), 6.64 (t, *J*=17.1 Hz, 1H), 5.30 (d, *J*=17.1 Hz, 1H), 5.22 - 5.10 (m, 1H), 4.95 (d, *J*=17.1 Hz, 1H), 4.47 - 4.35 (m, 1H), 4.33 - 4.23 (m, 1H), 1.33 (d, *J*=7.0 Hz, 3H).

Example 289:

(6S)-6-methyl-3-[5-(1-methylimidazol-2-yl)-2-oxo-oxazolidin-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of 1-(1-methyl-1H-imidazol-2-yl)-2-nitroethanol (compound 289b)

A mixture of 1-methyl-1H-imidazole-2-carbaldehyde (1.1 g, 10 mmol), barium hydroxide (171 mg, 1 mmol) and nitromethane (6.1 g, 100 mmol) in water (20 mL) was stirred for 2 hours at room temperature. The reaction mixture was extracted with EtOAc (50 mL) three times. The organic layers were combined, dried over Na_2SO_4 and concentrated *in vacuo* to give crude compound **289b** (1.5 g) as a yellow solid.

Preparation of 5-(1-methylimidazol-2-yl)oxazolidin-2-one (compound 289c)

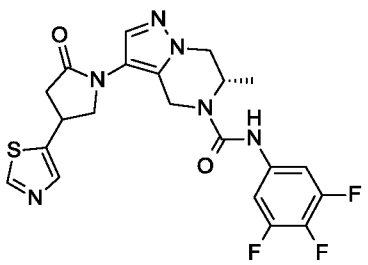
A mixture of 1-(1-methyl-1H-imidazol-2-yl)-2-nitroethanol (compound **289b**, 1.5 g, 8.76 mmol), hydrochloric acid (1.75 mL, 1M) and Pd/C (187 mg, 1.75 mmol) in ethanol (20 mL) was stirred at 50 °C for 16 hours under hydrogen balloon. The reaction mixture was filtered through celite and the filtrate was concentrated. The residue was dissolved in DCM (20 mL), to which was added triethylamine (887 mg, 8.76 mmol), and triphosgene (1.04 g, 3.51 mmol) slowly at room temperature. After stirred at room temperature for 30 mins, the reaction mixture was concentrated in *vacuo*. The resulting residue was purified by flash chromatography (silica gel, 10% MeOH in EtOAc) to give compound **289c** as yellow solid (200 mg). LCMS ($M+H^+$): 168.

Preparation of (6S)-6-methyl-3-[5-(1-methylimidazol-2-yl)-2-oxo-oxazolidin-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 289)

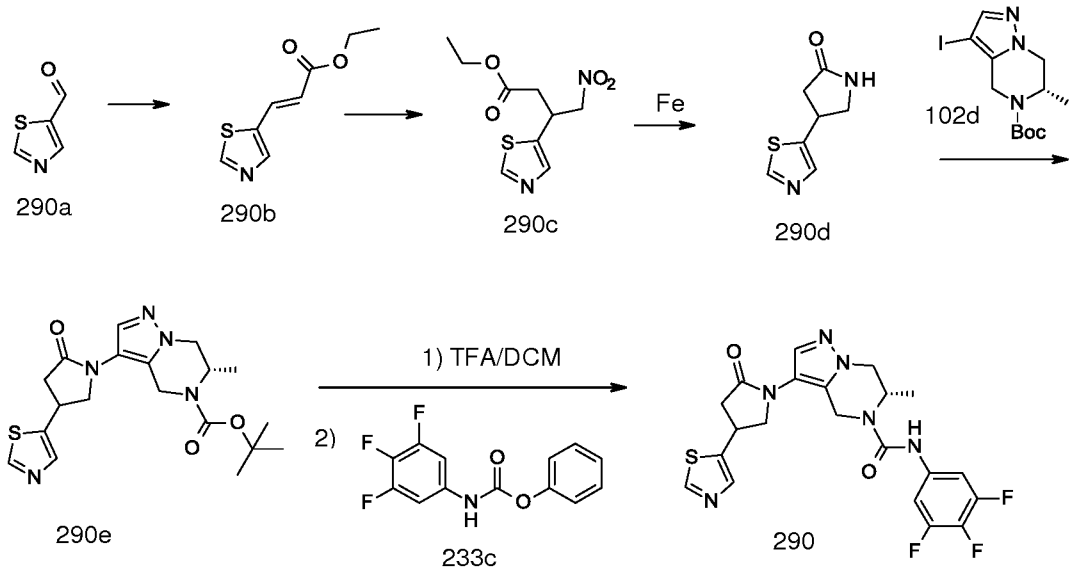
The title compound was prepared in analogy to **Example 262** by using 5-(1-methylimidazol-2-yl)oxazolidin-2-one (compound **289c**) instead of (S)-3-hydroxypyrrolidin-2-one. **Example 289** was obtained as a white solid (83 mg). LCMS ($M+H^+$): 476. ^1H NMR (400MHz, MeOD) δ ppm 7.75 (d, *J*=4.0 Hz, 1H), 7.34 - 7.30 (m, 2H), 7.25 (s, 1H), 7.07 (s, 1H), 6.05 - 6.00 (m, 1H), 5.13 (dd, *J*=9.9, 16.8 Hz, 1H), 5.06 - 4.95 (m, 1H), 4.71 - 4.53 (m, 2H), 4.43 - 4.28 (m, 2H), 4.22 - 4.13 (m, 1H), 3.86 (s, 3H), 1.29 - 1.26 (m, 3H).

Example 290:

(6S)-6-methyl-3-(2-oxo-4-thiazol-5-yl-pyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of ethyl 3-(thiazol-5-yl)acrylate (compound 290b)

A mixture of thiazole-5-carbaldehyde (1.13 g, 10 mmol) and ethyl 2-(triphenylphosphoranylidene)acetate (3.48 g, 10 mmol) in THF (30 mL) was stirred at room temperature for 30 minutes. The reaction mixture was concentrated in *vacuo*. The crude product was purified by flash chromatography (silica gel, 20% to 30% EtOAc in hexanes) to give compound **290b** as a colorless oil (1.8 g). LCMS ($M+H^+$): 184.

Preparation of ethyl 4-nitro-3-(thiazol-5-yl)butanoate (compound 290c)

A mixture of ethyl 3-(thiazol-5-yl)acrylate (compound **290b**, 0.91 g, 4.97 mmol), DBU (1.51 g, 9.93 mmol) and nitromethane (3.03 g, 49.7 mmol) in EtOH (20 mL) was stirred at 80 °C for 15 hours. The reaction mixture was concentrated in *vacuo*. The crude product was purified by flash chromatography (silica gel, 10% to 30% EtOAc in hexanes) to give compound **290c** as a light yellow oil (600 mg). LCMS ($M+H^+$): 245.

Preparation of 4-thiazol-5-ylpyrrolidin-2-one (compound 290d)

A mixture of ethyl 4-nitro-3-(thiazol-5-yl)butanoate (366 mg, 1.5 mmol), Fe (418 mg, 7.49 mmol) and ammonium chloride (401 mg, 7.49 mmol) in EtOH (10 mL)/water (2 mL) was stirred at 80 °C for 1 hour. The reaction mixture was filtered through celite and the filtrate was concentrated in *vacuo*. The crude product was purified by flash chromatography (silica gel, 10% MeOH in DCM) to give compound **290d** as light yellow oil (150 mg). LCMS ($M+H^+$): 169.

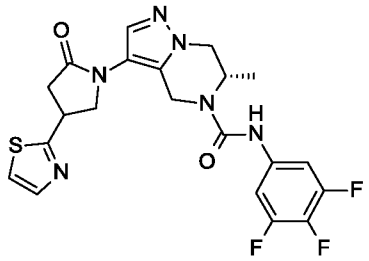
Preparation of (6S)-6-methyl-3-(2-oxo-4-thiazol-5-yl-pyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 290)

The title compound was prepared in analogy to **Example 262** by using 4-thiazol-5-ylpyrrolidin-2-one (compound **290d**) instead of (S)-3-hydroxypyrrolidin-2-one. **Example 290**

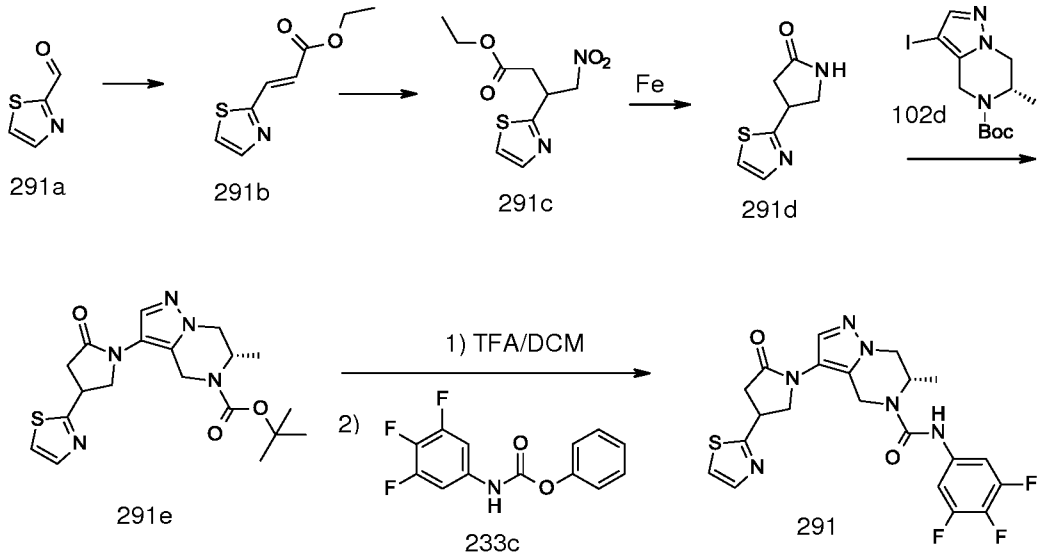
was obtained as a white solid (30 mg). LCMS ($M+H^+$): 477. ^1H NMR (400MHz, MeOD) δ ppm 8.97 (d, *J*=3.0 Hz, 1H), 7.88 (s, 1H), 7.66 (s, 1H), 7.34-7.25 (m, 2H), 5.08 (dd, *J*=4.4, 16.9 Hz, 1H), 4.98 - 4.92 (m, 1H), 4.53 (dd, *J*=5.6, 16.9 Hz, 1H), 4.36 - 4.23 (m, 3H), 4.17 (d, *J*=12.5 Hz, 1H), 3.97 - 3.88 (m, 1H), 3.09 (dd, *J*=8.0, 17.1 Hz, 1H), 2.75 (dd, *J*=7.2, 17.2 Hz, 1H), 1.30 - 1.26 (m, 3H).

Example 291:

(6S)-6-methyl-3-(2-oxo-4-thiazol-2-yl-pyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of 4-thiazol-2-ylpyrrolidin-2-one (compound 291d)

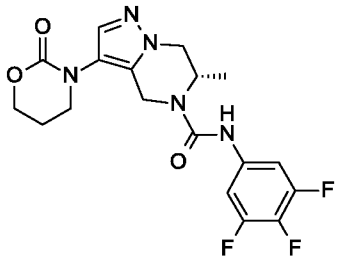
Compound **291d** was prepared in analogy to compound **290d** by using thiazole-2-carbaldehyde instead of thiazole-5-carbaldehyde. Compound **291d** was obtained as a light yellow oil (150 mg). LCMS ($M+H^+$): 169.

Preparation of (6S)-6-methyl-3-(2-oxo-4-thiazol-2-yl-pyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 291)

The title compound was prepared in analogy to Example **262** by using 4-thiazol-2-ylpyrrolidin-2-one (compound **291d**) instead of (S)-3-hydroxypyrrolidin-2-one. **Example 291** was obtained as a white solid (7 mg). LCMS ($M+H^+$): 477. ^{1}H NMR (400MHz, MeOD) δ ppm 7.81 (d, *J*=3.0 Hz, 0.5H), 7.79 (d, *J*=3.0 Hz, 0.5H), 7.66 (s, 0.5H), 7.65 (s, 0.5H), 7.58 (d, *J*=3.6 Hz, 0.5H), 7.56 (d, *J*=3.6 Hz, 0.5H), 7.36 - 7.23 (m, 2H), 5.07 (dd, *J*=2.5, 16.8 Hz, 1H), 5.01 - 4.94 (m, 1H), 4.53 (dd, *J*=2.1, 16.9 Hz, 1H), 4.37 - 4.25 (m, 3H), 4.20 - 4.13 (m, 1H), 4.12 - 4.03 (m, 1H), 3.12 (dd, *J*=8.8, 17.1 Hz, 1H), 2.97 - 2.87 (m, 1H), 1.29 - 1.26 (m, 3H).

Example 292:

(6S)-6-methyl-3-(2-oxo-1,3-oxazinan-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

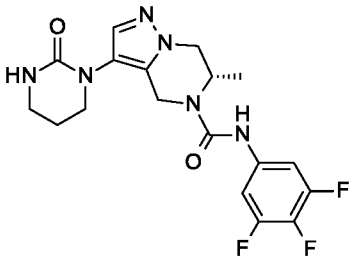


Preparation of (6S)-6-methyl-3-(2-oxo-1,3-oxazinan-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 292)

The title compound was prepared in analogy to **Example 223** by using 1,3-oxazinan-2-one instead of pyrrolidin-2-one and phenyl N-(3,4,5-trifluoro-phenyl)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 292** was obtained as a white solid (25 mg). LCMS ($M+H^+$): 410. ^{1}H NMR (400MHz, MeOD) δ ppm 7.64 (s, 1H), 7.33-7.27 (m, 2H), 5.02 - 4.92 (m, 2H), 4.51 - 4.39 (m, 3H), 4.35 - 4.24 (m, 1H), 4.16 (dd, *J*=1.0, 12.8 Hz, 1H), 3.84 - 3.66 (m, 2H), 2.23 (q, *J*=5.8 Hz, 2H), 1.26 (d, *J*=7.0 Hz, 3H).

Example 293:

(6S)-6-methyl-3-(2-oxohexahydropyrimidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

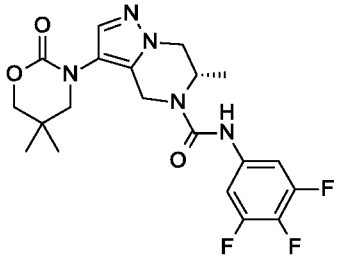


Preparation of (6S)-6-methyl-3-(2-oxohexahydropyrimidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 293)

The title compound was prepared in analogy to **Example 223** by using hexahydropyrimidin-2-one instead of pyrrolidin-2-one and phenyl N-(3,4,5-trifluoro-phenyl)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 293** was obtained as a white solid (7 mg). LCMS ($M+H^+$): 409. ^{1}H NMR (400MHz, MeOD) δ ppm 7.55 (s, 1H), 7.34-7.28 (m, 2H), 5.01 - 4.91 (m, 2H), 4.44 (d, *J*=16.6 Hz, 1H), 4.32 - 4.23 (m, 1H), 4.18 - 4.09 (m, 1H), 3.68 (t, *J*=5.8 Hz, 2H), 3.40 (t, *J*=5.8 Hz, 2H), 2.10 (q, *J*=5.8 Hz, 2H), 1.26 (d, *J*=7.0 Hz, 3H).

Example 294:

(6S)-3-(5,5-dimethyl-2-oxo-1,3-oxazinan-3-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

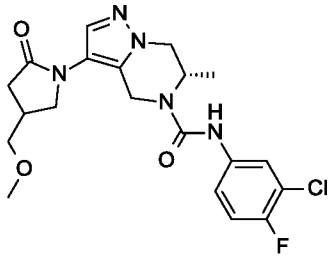


Preparation of (6S)-3-(5,5-dimethyl-2-oxo-1,3-oxazinan-3-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 294)

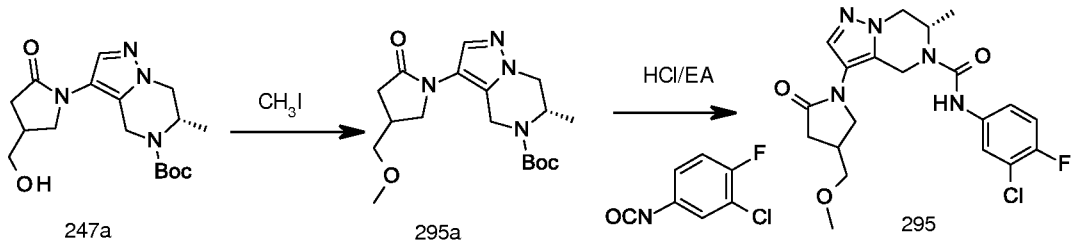
The title compound was prepared in analogy to **Example 223** by using 5,5-dimethyl-1,3-oxazinan-2-one instead of pyrrolidin-2-one and phenyl N-(3,4,5-trifluoro-phenyl)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 294** was obtained as a white solid (16 mg). LCMS ($M+H^+$): 438. ^{1}H NMR (400MHz, MeOD) δ ppm 7.61 (s, 1H), 7.32-7.24(m, 2H), 5.00 - 4.93 (m, 2H), 4.42 (d, *J*=16.8 Hz, 1H), 4.30 (dd, *J*=4.4, 12.4 Hz, 1H), 4.21 - 4.10 (m, 3H), 3.54 - 3.44 (m, 2H), 1.26 (d, *J*=7.0 Hz, 3H), 1.21 (s, 3H), 1.20 (s, 3H).

Example 295

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-[4-(methoxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: preparation of tert-butyl (6S)-3-[4-(methoxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 295a)

To a solution of tert-butyl (6S)-3-[4-(hydroxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **247a**, 50 mg, 0.143 mmol) in THF (5 mL) was added NaH (8.3 mg, 0.215 mmol, 60%) and then CH_3I (40.6 mg, 0.286 mmol) at 0°C . The reaction mixture was stirred at room temperature for 48 hours. Then the reaction was quenched with H_2O and extracted with EtOAc (20 mL). The organic phase was dried over Na_2SO_4 and then concentrated to give crude compound **295a**, which was used in next step without further purification. LCMS ($M+H^+$)**:** 365.

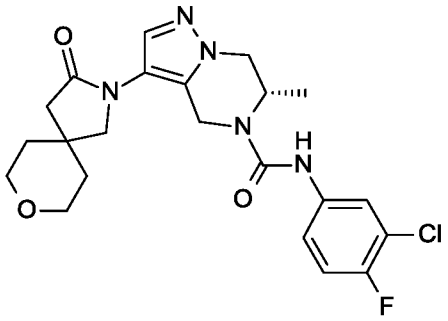
Step 2: preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-3-[4-(methoxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 295)

The title compound was prepared in analogy to **Example 246** by using tert-butyl (6S)-3-[4-(methoxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **295a**) instead of tert-butyl (6S)-3-(3,6-dioxo-4,7,8,8a-tetrahydro-1H-pyrrolo[1,2-a]pyrazin-2-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **246f**). **Example 295** was obtained as a white solid (8 mg). LCMS ($M+H^+$): 436. ^{1}HNMR: (400MHz, DMSO-d_6) δ ppm 8.95 (d, *J*=2.3 Hz, 1H), 7.73 (dd, *J*=2.4, 6.9 Hz, 1H), 7.60 (d, *J*=2.3 Hz, 1H), 7.42 (d, *J*=8.8 Hz, 1H), 7.37 - 7.28 (m, 1H), 4.97 (dd, *J*=2.4, 17.2 Hz, 1H),

4.91 - 4.81 (m, 1H), 4.36 (dd, *J*=5.5, 17.1 Hz, 1H), 4.23 - 4.16 (m, 1H), 4.14 - 4.07 (m, 1H), 3.91 - 3.75 (m, 1H), 3.56 - 3.44 (m, 1H), 3.40 (dd, *J*=4.0, 6.5 Hz, 2H), 3.29 (d, *J*=2.3 Hz, 3H), 2.81 - 2.65 (m, 2H), 2.20 (dd, *J*=6.7, 16.9 Hz, 1H), 1.14 (d, *J*=6.5 Hz, 3H).

Example 296

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(3-oxo-8-oxa-2-azaspiro[4.5]decan-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

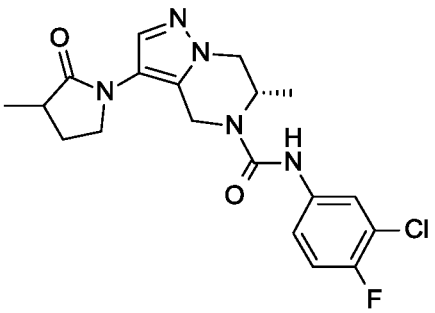


Preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(3-oxo-8-oxa-2-azaspiro[4.5]decan-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 296)

The title compound was prepared in analogy to **Example 246** by using 8-oxa-2-azaspiro[4.5]decan-3-one instead of 1,2,4,7,8,8a-hexahydropyrrolo[1,2-a]pyrazine-3,6-dione (compound **246e**). **Example 296** was obtained as a white solid (24.3 mg). LCMS: ($M+H^+$): 462. ^{1}H NMR (400MHz, METHANOL-d_4) δ ppm 7.62 (s, 1H), 7.59 (dd, *J*=2.6, 6.7 Hz, 1H), 7.32 (ddd, *J*=2.8, 4.1, 9.0 Hz, 1H), 7.19 - 7.12 (m, 1H), 5.05 - 4.91 (m, 2H), 4.48 (d, *J*=17.1 Hz, 1H), 4.28 (dd, *J*=4.5, 12.7 Hz, 1H), 4.19 - 4.09 (m, 1H), 3.79 - 3.67 (m, 6H), 2.54 (s, 2H), 1.83 - 1.70 (m, 4H), 1.26 (d, *J*=6.8 Hz, 3H).

Example 297

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(3-methyl-2-oxo-pyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

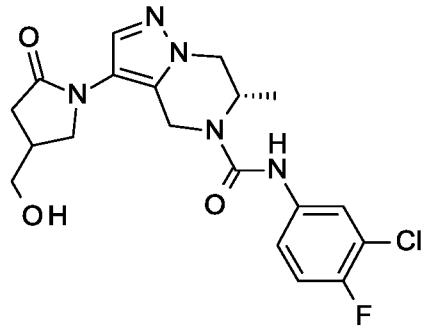


Preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(3-methyl-2-oxo-pyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 297)

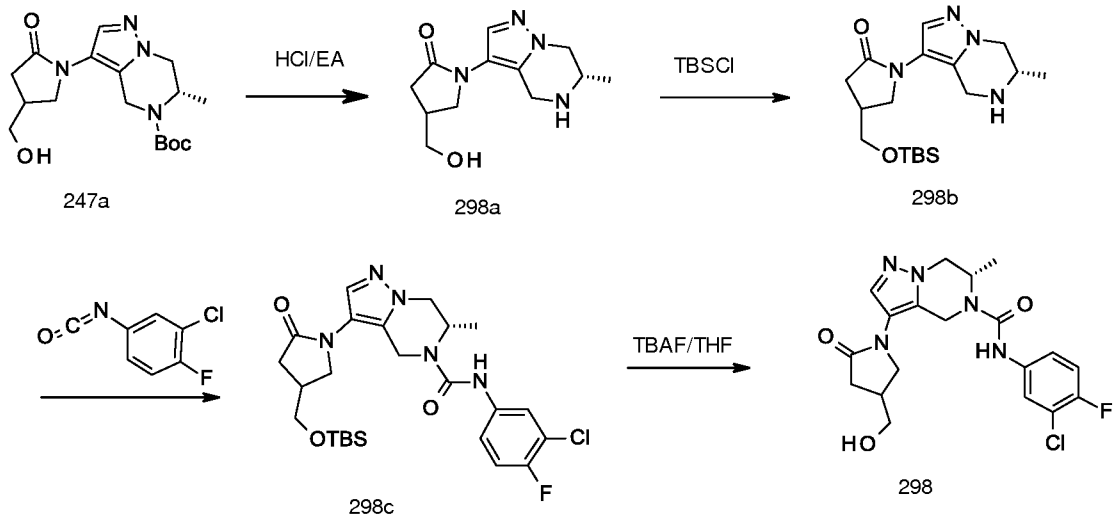
The title compound was prepared in analogy to Example **246** by using 3-methylpyrrolidin-2-one instead of 1,2,4,7,8,8a-hexahydropyrrolo[1,2-a]pyrazine-3,6-dione (compound **246e**). Example **297** was obtained as a white solid (28.7 mg). LCMS ($M+H^+$): 406. ^1H NMR (400MHz, DMSO-d_6) δ ppm 8.95 (d, *J*=4.8 Hz, 1H), 7.74 (dd, *J*=1.8, 6.5 Hz, 1H), 7.62 (d, *J*=2.3 Hz, 1H), 7.46 - 7.39 (m, 1H), 7.35 - 7.28 (m, 1H), 4.99 (dd, *J*=9.5, 17.1 Hz, 1H), 4.90 - 4.81 (m, 1H), 4.44 - 4.34 (m, 2H), 4.25 - 4.16 (m, 1H), 4.15 - 4.07 (m, 1H), 3.77 - 3.68 (m, 1H), 3.68 - 3.60 (m, 1H), 2.38 - 2.28 (m, 1H), 1.79 - 1.67 (m, 1H), 1.23 - 1.08 (m, 6H).

Example 298

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-[4-(hydroxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: preparation of 4-(hydroxymethyl)-1-[(6S)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl]pyrrolidin-2-one (compound 298a)

A solution of tert-butyl (6S)-3-[4-(hydroxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **247a**, 400.0 mg, 1.14 mmol) in HCl/EtOAc (5.0 mL, 1M) was stirred at 25°C for 1 hour. Then the reaction mixture was concentrated *in vacuo* to provide crude compound **298a** (500 mg), which was used directly in the next step without further purification.

Step 2: preparation of 4-[[tert-butyl(dimethyl)silyl]oxymethyl]-1-[(6S)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl]pyrrolidin-2-one (compound 298b)

To a solution of 4-(hydroxymethyl)-1-[(6S)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl]pyrrolidin-2-one (compound **298a**, 100.0 mg, 0.35 mmol) in DCM (15 mL) was added imidazole (142.97 mg 2.1 mmol) and TBSCl (79.53 mg, 0.53 mmol) under N_2, then the reaction mixture was stirred at room temperature for 12 hours. The reaction mixture was partitioned between H_2O (30 mL) and EtOAc (50 mL). The organic phase was separated and concentrated. The obtained residue was purified by silica gel column chromatography (DCM: MeOH=50:1 to 10:1) to give compound **298b** (100.0 mg). LCMS ($M+H^+$): 365.

Step 3: preparation of (6S)-3-[4-[[tert-butyl(dimethyl)silyl]oxymethyl]-2-oxo-pyrrolidin-1-yl]-N-(3-chloro-4-fluoro-phenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (compound 298c)

To a solution of 4-[[tert-butyl(dimethyl)silyl]oxymethyl]-1-[(6S)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl]pyrrolidin-2-one (compound **298b**, 100.0 mg, 0.28 mmol) in DCM (5.0 mL) was added DIPEA (108.36 mg 0.84 mmol) and 2-chloro-1-fluoro-4-isocyanato-benzene (58.33 mg 0.34 mmol) at 0 °C, then the reaction was stirred at room temperature for 12 hours. The reaction mixture was partitioned between H_2O (20 mL) and DCM

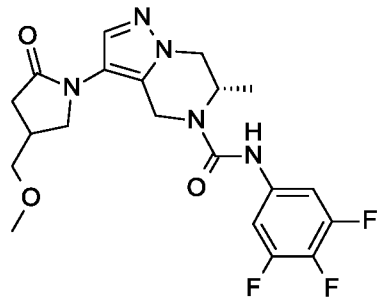
(20 mL). The organic phase was separated and concentrated *in vacuo* to give crude compound **298c** (110 mg). LCMS ($M+H^+$): 536.

Step 4: preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-3-[4-(hydroxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 298)

To a solution of (6S)-3-[4-[[tert-butyl(dimethyl)silyl]oxymethyl]-2-oxo-pyrrolidin-1-yl]-N-(3-chloro-4-fluoro-phenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (compound **298c**, 110.0 mg, 0.21 mmol) in THF (5.0 mL) was added a solution of TBAF in THF (0.32 mL, 0.32 mmol). The reaction mixture was stirred at room temperature for 12 hours, then diluted with EtOAc, and washed with brine. The organic layer was concentrated, and the residue was purified by silica gel column chromatography (DCM: MeOH=100:1 to 60:1) to provide **Example 298** (25 mg). LCMS ($M+H^+$): 422. ^{1}H NMR (400MHz, MeOH) δ ppm 7.69 - 7.57 (m, 2H), 7.34 (td, *J*=3.5, 8.5 Hz, 1H), 7.21 - 7.14 (m, 1H), 5.03 (dd, *J*=2.3, 16.8 Hz, 1H), 5.00 - 4.94 (m, 1H), 4.51 (d, *J*=16.8 Hz, 1H), 4.30 (dd, *J*=4.4, 12.7 Hz, 1H), 4.19 - 4.13 (m, 1H), 3.96 (td, *J*=8.9, 13.1 Hz, 1H), 3.74 - 3.61 (m, 3H), 2.79 - 2.63 (m, 2H), 2.45 - 2.37 (m, 1H), 1.32 - 1.23 (m, 3H).

Example 299

(6S)-3-[4-(methoxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



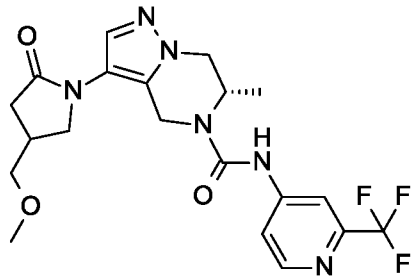
Preparation of (6S)-3-[4-(methoxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 297)

The title compound was prepared in analogy to the preparation of **Example 11** by 3,4,5-trifluoroaniline instead of 3-(trifluoromethyl)aniline and tert-butyl (6S)-3-[4-(methoxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **295a**) instead of tert-butyl 3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **11a**). **Example 299** was obtained as white solid (10.5 mg).

LCMS: (M+H$^+$): 438. ^{1}H NMR (400MHz, MeOD) δ ppm 7.63 (s, 1H), 7.34 - 7.21 (m, 2H), 5.03 (d, *J*=16.9 Hz, 1H), 4.99 - 4.94 (m, 1H), 4.49 (dd, *J*=1.8, 16.9 Hz, 1H), 4.35 - 4.25 (m, 1H), 4.16 (dd, *J*=1.1, 12.7 Hz, 1H), 3.96 (ddd, *J*=8.2, 9.7, 15.6 Hz, 1H), 3.71 - 3.61 (m, 1H), 3.54 - 3.46 (m, 2H), 3.41 (d, *J*=1.1 Hz, 3H), 2.90 - 2.78 (m, 1H), 2.74 - 2.64 (m, 1H), 2.40 (dd, *J*=6.3, 17.2 Hz, 1H), 1.27 (d, *J*=6.9 Hz, 3H).

Example 300

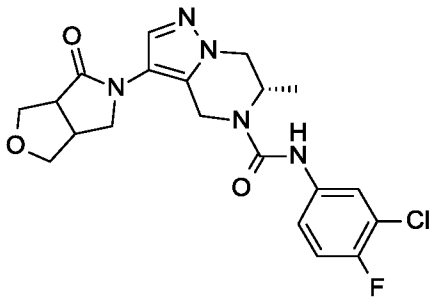
(6S)-3-[4-(methoxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-[2-(trifluoromethyl)-4-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



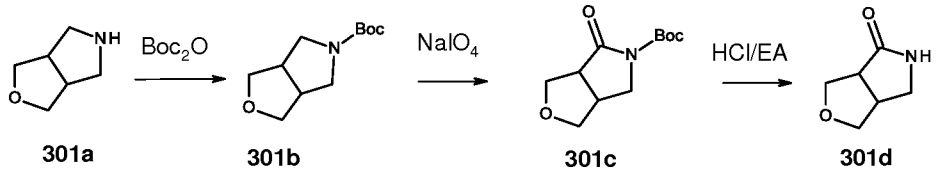
To a mixture of 2-(trifluoromethyl)pyridin-4-amine (29.7 mg, 0.18 mmol) and pyridine (66.4 mg, 0.83 mmol) in THF (5.0 mL) was added phenyl chloroformate (28.6 mg, 0.18 mmol) under N_2 at 0 °C. The reaction mixture was stirred at room temperature for 2 hours, then concentrated. To the resulting residue was added DMF (2.5 mL), tert-butyl (6S)-3-[4-(methoxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **295a**, 50.0 mg, 0.166 mmol) and DPIEA (0.2 mL), and the reaction mixture was stirred at 100 °C for 2 hours. Then the reaction mixture was purified by Prep-HPLC to give **Example 300** as a white solid (27.6 mg). LCMS: (M+H$^+$): 453. ^{1}H NMR (400MHz, MeOH) δ ppm 8.49 (d, *J*=5.6 Hz, 1H), 8.02 (s, 1H), 7.76 (d, *J*=5.6 Hz, 1H), 7.63 (s, 1H), 5.10 (d, *J*=16.9 Hz, 1H), 5.05 - 4.96 (m, 1H), 4.54 (dd, *J*=2.3, 17.0 Hz, 1H), 4.33 (dd, *J*=2.4, 12.8 Hz, 1H), 4.17 (d, *J*=12.7 Hz, 1H), 3.96 (ddd, *J*=8.2, 9.7, 14.8 Hz, 1H), 3.66 (ddd, *J*=5.5, 9.8, 13.3 Hz, 1H), 3.56 - 3.47 (m, 2H), 3.41 (d, *J*=1.3 Hz, 3H), 2.91 - 2.79 (m, 1H), 2.75 - 2.65 (m, 1H), 2.41 (dd, *J*=6.1, 17.2 Hz, 1H), 1.30 (d, *J*=6.8 Hz, 3H).

Example 301

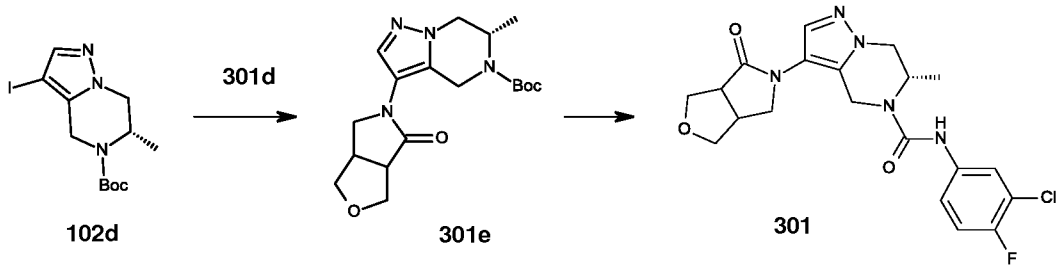
(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(4-oxo-3,3a,6,6a-tetrahydro-1H-furo[3,4-c]pyrrol-5-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



301a 301b 301c 301d



102d 301e 301

Preparation of tert-butyl 1,3,3a,4,6,6a-hexahydrofuro[3,4-c]pyrrole-5-carboxylate (compound 301b)

To a solution of 3,3a,4,5,6,6a-hexahydro-1H-furo[3,4-c]pyrrole **301a** (298.1 mg, 2.0 mmol) and Et_3N (607.2 mg, 6.0 mmol) in DCM (10.0 mL) was added Boc_2O (481.0 mg, 2.2 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 2 hours, and then washed with water (10 mL). The organic phase was concentrated to afford compound **301b** as colorless oil (400 mg). LCMS ($M+H^+$): 338

Preparation of tert-butyl 4-oxo-3,3a,6,6a-tetrahydro-1H-furo[3,4-c]pyrrole-5-carboxylate (compound 301c)

To a solution of tert-butyl 1,3,3a,4,6,6a-hexahydrofuro[3,4-c]pyrrole-5-carboxylate (compound **301b**, 400.0 mg, 1.88 mmol) in EtOAc (6.0 mL) was added $NaIO_4$ (1.9 g, 8.8 mmol) in H_2O (20 mL) and RuO_2 (75.6 mg, 0.564 mmol). The reaction mixture was stirred at room temperature for 24 hours. The organic phase was separated and the aqueous phase was extracted with ethyl acetate (20 mL). The organic phase was treated with isopropyl alcohol (2.0 mL), and then washed with brine and concentrated to afford compound **301c** as colorless oil (400 mg). LCMS ($M+H^+$): 228

Preparation of 1,3,3a,5,6,6a-hexahydrofuro[3,4-c]pyrrol-4-one (compound 301d)

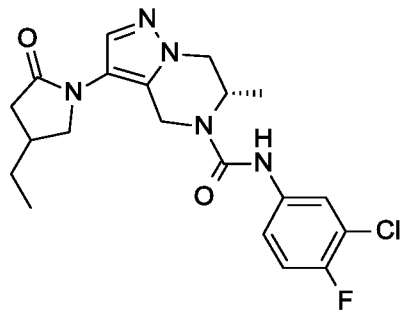
A mixture of tert-butyl 4-oxo-3,3a,6,6a-tetrahydro-1H-furo[3,4-c]pyrrole-5-carboxylate (compound **301c**, 400.0 mg, 1.76 mmol) in HCl/EtOAc (5.0 mL) was stirred at room temperature for 1 hour. The reaction mixture was concentrated to afford compound **301d** as a colorless oil (218 mg). LCMS ($M+H^+$): 128

Preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(4-oxo-3,3a,6,6a-tetrahydro-1H-furo[3,4-c]pyrrol-5-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 301)

The title compound was prepared in analogy to **Example 246** by using 1,3,3a,5,6,6a-hexahydrofuro[3,4-c]pyrrol-4-one (compound **301d**) instead of 1,2,4,7,8,8a-hexahydropyrrolo[1,2-a]pyrazine-3,6-dione (compound **246e**). **Example 301** was obtained as white solid (16 mg). LCMS ($M+H^+$): 434. ^{1}H NMR (300MHz, MeOD) δ ppm 7.80 (s, 1H), 7.62-7.58 (m, 1H), 7.34-7.31 (m, 1H), 7.18-7.12 (m, 1H), 5.07-4.92 (m, 2H), 4.75-4.71 (m, 1H), 4.53-4.49 (m, 1H), 4.32-4.16 (m, 4H), 3.92-3.80 (m, 3H), 3.67-3.61 (m, 1H), 3.20-3.16 (m, 1H), 1.27 (d, *J*=7.0 Hz, 3H).

Example 302

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-ethyl-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



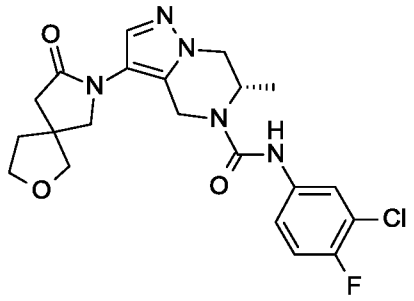
Preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-ethyl-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 302)

The title compound was prepared in analogy to **Example 246** by using 4-ethylpyrrolidin-2-one instead of 1,2,4,7,8,8a-hexahydropyrrolo[1,2-a]pyrazine-3,6-dione (compound **246e**). **Example 302** was obtained as white solid (27 mg). LCMS ($M+H^+$): 420.0. ^{1}H NMR (400MHz, MeOD) δ ppm 7.66 - 7.56 (m, 2H), 7.36 - 7.30 (m, 1H), 7.16 (t, 1H), 5.06 - 4.98 (m, 1H), 4.98 - 4.92 (m, 1H), 4.50 (m, 1H), 4.34 - 4.24 (m, 1H), 4.20 - 4.11 (m, 1H), 3.93 (dd, *J*=8.0, 9.6, 14.4

Hz, 1H), 3.53 (dd, *J*=6.9, 9.6, 13.2 Hz, 1H), 2.68 (dd, *J*=8.7, 16.8 Hz, 1H), 2.56 - 2.44 (m, 1H), 2.33 - 2.22 (m, 1H), 1.67 - 1.55 (m, 2H), 1.28-1.24 (m, 3H), 1.01 (t, *J*=7.4 Hz, 3H).

Example 303

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(8-oxo-2-oxa-7-azaspiro[4.4]nonan-7-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

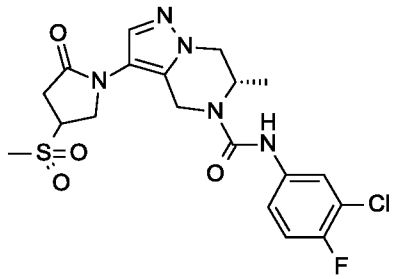


Preparation of Example 303

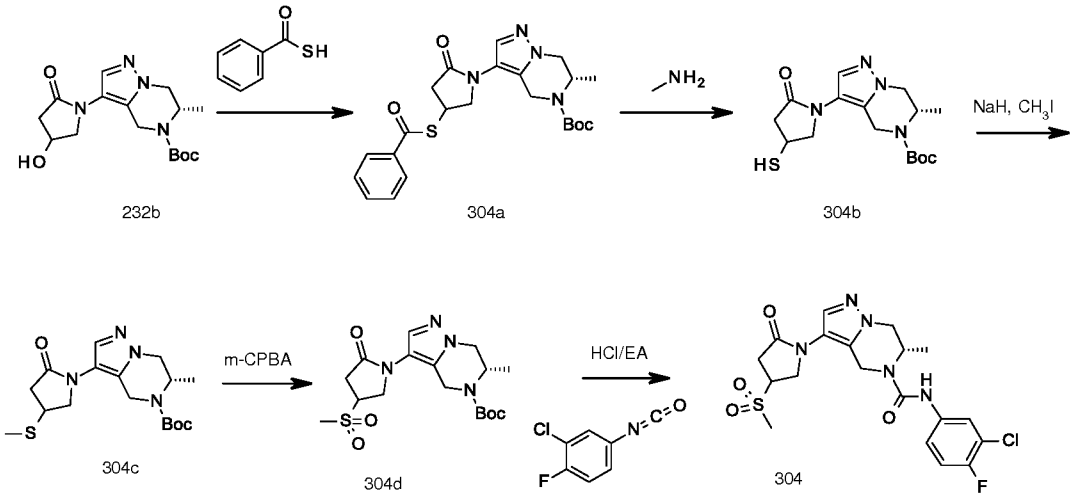
The title compound was prepared in analogy to **Example 246** by using 4- 2-oxa-7-azaspiro[4.4]nonane instead of 1,2,4,7,8,8a-hexahydropyrrolo[1,2-a]pyrazine-3,6-dione (compound **246e**). **Example 303** was obtained as brown solid (8 mg). LCMS: ($M+H^+$): 448. ^1H NMR (400MHz, MeOD) δ ppm 7.65 (s, 1H), 7.62 (dd, *J*=2.5, 6.5 Hz, 1H), 7.37 - 7.31 (m, 1H), 7.18 (t, *J*=9.0 Hz, 1H), 5.04 (dd, *J*=4.3, 17.1 Hz, 1H), 4.52 (dd, *J*=3.5, 16.8 Hz, 1H), 4.30 (dd, *J*=4.4, 12.7 Hz, 1H), 4.16 (d, *J*=12.8 Hz, 1H), 3.97 (t, *J*=7.2 Hz, 2H), 3.84 (dd, *J*=3.1, 7.4 Hz, 2H), 3.73 (d, *J*=8.3 Hz, 1H), 3.37 (s, 2H), 2.67 (s, 2H), 2.20 - 2.09 (m, 2H), 1.32 - 1.25 (m, 3H).

Example 304

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(4-methylsulfonyl-2-oxo-pyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: preparation of tert-butyl (6S)-3-(4-benzoylsulfanyl-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 304a)

To a solution of PPh_3 (290.8 mg, 1.11 mmol) in THF (10.0 mL) was added DEAD (193.1 mg, 1.11 mmol) at 0 °C under N_2 and the reaction mixture was stirred at 0 °C for 10 mins, then tert-butyl (6S)-3-(4-hydroxy-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **232b**, 250.0 mg, 0.74 mmol) and benzenecarbothioic S-acid (204.2 mg, 1.48 mmol) were added. The reaction mixture was stirred for 24 hours at room temperature, and then was purified by prep-HPLC to afford compound **304a** as white solid (200 mg). LCMS ($M+H^+$): 457

Step 2: preparation of tert-butyl (6S)-6-methyl-3-(2-oxo-4-sulfanyl-pyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 304b)

To a solution of tert-butyl (6S)-3-(4-benzoylsulfanyl-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **304a**, 100.0 mg, 0.22 mmol) in MeOH (2.0 mL) was added methylamine (4.40 mL, 1M in THF) at room temperature under N_2 and the reaction mixture was stirred at same temperature for 1 hour. The reaction mixture was concentrated to give crude compound **304b** as a white solid (100 mg). LCMS: ($M+H^+$): 353.

Step 3: preparation of tert-butyl (6S)-6-methyl-3-(4-methylsulfanyl-2-oxo-pyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 304c)

To a solution of tert-butyl (6S)-6-methyl-3-(2-oxo-4-sulfanyl-pyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **304b**, 100.0 mg, 0.28 mmol) in DMF (2.0 mL) was added NaH (56.0 mg, 1.4 mmol) at 0 °C under N_2 and then CH_3I (397.6 mg, 2.8 mmol). The reaction mixture was then allowed to stir at room temperature for 1 hour. The reaction mixture was filtered and the filtrate was purified by prep-HPLC to afford compound **304c** as a white solid (30 mg). LCMS ($M+H^+$): 367.

Step 4: preparation of tert-butyl (6S)-6-methyl-3-(4-methylsulfonyl-2-oxo-pyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 304d)

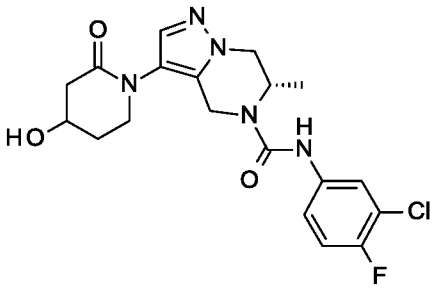
To a solution of tert-butyl (6S)-6-methyl-3-(4-methylsulfanyl-2-oxo-pyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **304c**, 30.0 mg, 0.081 mmol) in DCM (2.0 mL) was added m-CPBA (17.4 mg, 0.081 mmol) at room temperature. The reaction mixture was stirred at room temperature for 1 hour, and then washed with aqueous sodium sulfite solution. The organic phase was dried over Na_2SO_4, and concentrated to afford crude compound **304d** as a white solid (24 mg). LCMS ($M+H^+$): 399.

Preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(4-methylsulfonyl-2-oxo-pyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 304)

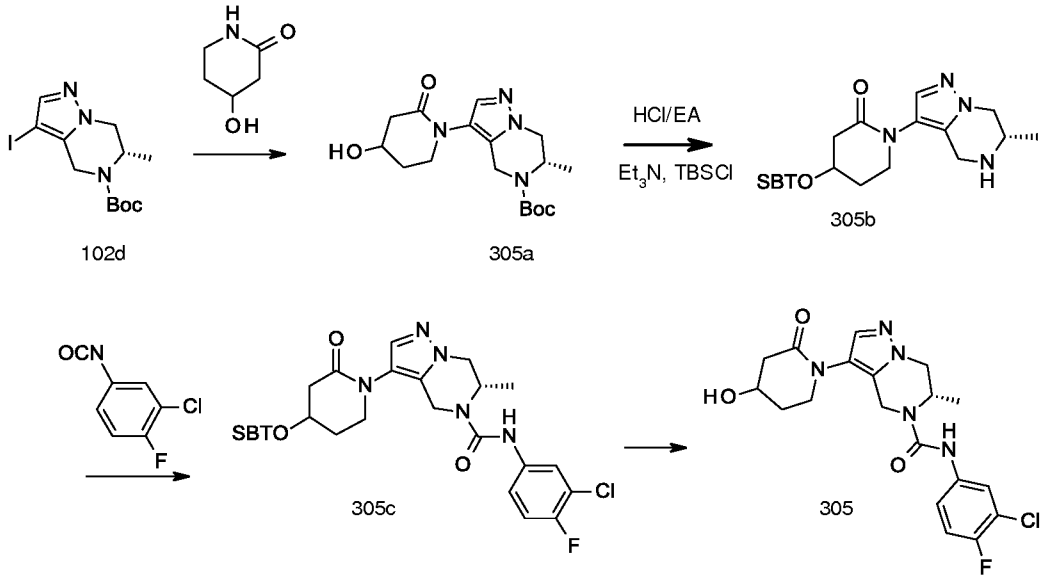
The title compound was prepared in analogy to Example **246** by using tert-butyl (6S)-6-methyl-3-(4-methylsulfonyl-2-oxo-pyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **304d**) instead of tert-butyl (6S)-3-(3,6-dioxo-4,7,8,8a-tetrahydro-1H-pyrrolo[1,2-a]pyrazin-2-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **246f**). **Example 304** was obtained as white solid (3 mg). LCMS ($M+H^+$): 470. ^1H NMR (300MHz, MeOD) δ ppm 7.66 (s, 1H), 7.64 - 7.59 (m, 1H), 7.38 - 7.29 (m, 1H), 7.16 (s, 1H), 5.09 - 4.98 (m, 2H), 4.56 - 4.42 (m, 1H), 4.34 - 4.11 (m, 5H), 3.09 (d, *J*=1.1 Hz, 5H), 1.29-1.24 (m, 3H)

Example 305

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-hydroxy-2-oxo-1-piperidyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of tert-butyl (6S)-3-(4-hydroxy-2-oxo-1-piperidyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 305a)

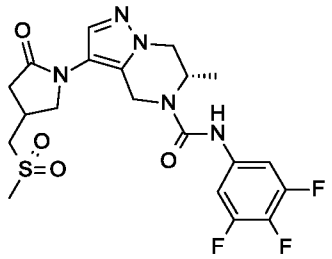
Compound **305a** was prepared in analogy to compound **246f** by using 4-hydroxypiperidin-2-one instead of 1,2,4,7,8,8a-hexahydropyrrolo[1,2-a]pyrazine-3,6-dione (compound **246e**). Compound **305a** was obtained as a white solid (270 mg). LCMS ($M+H^+$): 351.

Preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-hydroxy-2-oxo-1-piperidyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 305)

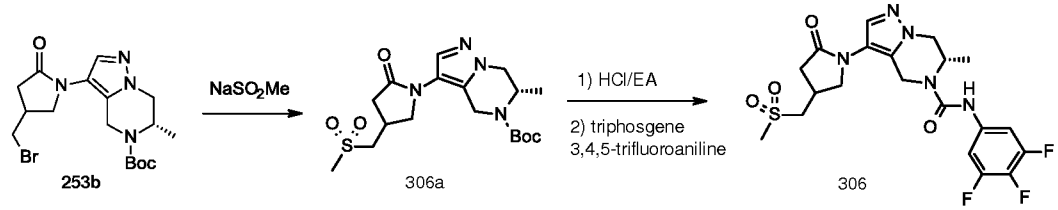
The title compound was prepared in analogy to Example **298** by using tert-butyl (6S)-3-(4-hydroxy-2-oxo-1-piperidyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **305a**) instead of 4-(hydroxymethyl)-1-[(6S)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl]pyrrolidin-2-one (compound **298a**). Example **305** was obtained as a white solid (8.7 mg). LCMS ($M+H^+$): 422. ^{1}H NMR (400 MHz, MeOD) δ ppm 7.88 (d, *J*=4.52 Hz, 1H), 7.64 (dd, *J*=6.52, 1.76 Hz, 1H), 7.32 - 7.39 (m, 1H), 7.17 (t, *J*=9.03 Hz, 1H), 4.98 - 5.00 (m, 2H), 4.20 - 4.46 (m, 4H), 3.82 - 4.00 (m, 1H), 3.61 - 3.77 (m, 1H), 2.83 (dt, *J*=17.69, 4.83 Hz, 1H), 2.53 (dt, *J*=17.57, 4.27 Hz, 1H), 1.97 - 2.25 (m, 2H), 1.29 (d, *J*=6.78 Hz, 3H).

Example 306

(6S)-6-methyl-3-[4-(methylsulfonylmethyl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: preparation of tert-butyl (6S)-6-methyl-3-[4-(methylsulfonylmethyl)-2-oxo-pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 306a)

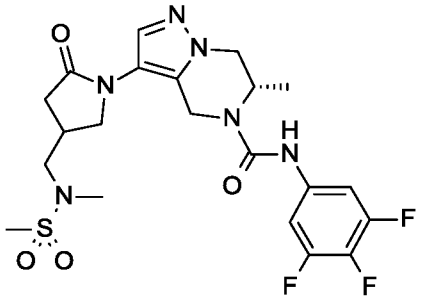
To a solution of tert-butyl (6S)-3-[4-(bromomethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **253b**, 50.0 mg, 0.12 mmol) in DMF (5.0 mL) was added CH_3SO_2Na (18.54 mg, 0.18 mmol), then the reaction was stirred at 110 °C for 12 hours. The reaction was concentrated and the crude product was purified by Prep-HPLC to give compound **306a** (30.0 mg) as white solid. LCMS ($M+H^+$): 413.

Step 2: preparation of (6S)-6-methyl-3-[4-(methylsulfonylmethyl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 306)

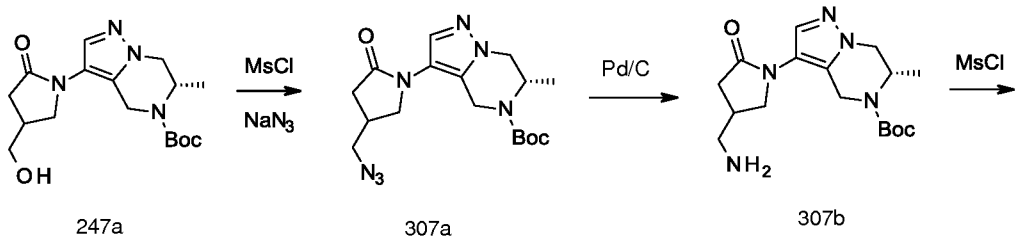
The title compound was prepared in analogy to the preparation of **Example 11** by 3,4,5-trifluoroaniline instead of 3-(trifluoromethyl)aniline and tert-butyl (6S)-6-methyl-3-[4-(methylsulfonylmethyl)-2-oxo-pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **306a**) instead of tert-butyl 3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **11a**). **Example 306** was obtained as a white solid (7 mg). LCMS ($M+H^+$): 486. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.15 (br. s., 1H), 8.47 (s, 1H), 7.58 (d, *J*=5.5 Hz, 1H), 7.43 (dd, *J*=6.5, 10.8 Hz, 1H), 4.97 (dd, *J*=11.3, 17.1 Hz, 1H), 4.85 (br. s., 1H), 4.41 - 4.31 (m, 1H), 4.25 - 4.08 (m, 2H), 3.99 - 3.84 (m, 1H), 3.71 - 3.58 (m, 1H), 3.47-3.43 (m, 1H), 3.21 - 3.13 (m, 2H), 3.10 - 2.88 (m, 3H), 2.65 (dd, *J*=8.7, 16.7 Hz, 1H), 2.45 - 2.33 (m, 1H), 1.22 - 0.99 (m, 3H).

Example 307

(6S)-6-methyl-3-[4-[[methyl(methylsulfonyl)amino]methyl]-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: preparation of tert-butyl (6S)-3-[4-(azidomethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 307a)

To a solution of tert-butyl (6S)-3-[4-(hydroxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **247a**, 300.0 mg, 0.86 mmol) in DCM (10 mL) was added TEA (260.58 mg, 2.58 mmol) and MsCl (117.37 mg 1.03 mmol). After stirred at room temperature for 6 hours, the reaction mixture was concentrated. The obtained residue was dissolved in DMF (5.0 mL), to which was added NaN_3 (46.15 mg 0.71 mmol). Then the reaction mixture was stirred at 120 °C for 12 hours and concentrated, then the crude product was purified by Prep-HPLC to give compound **307a** as a white solid(150 mg). LCMS ($M+H^+$): 376.

Step 2: preparation of tert-butyl (6S)-3-[4-(aminomethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 307b)

To a solution of tert-butyl (6S)-3-[4-(azidomethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **307a**,150.0 mg, 0.4 mmol) in

MeOH/THF (15 mL, v/v=1:1) was added 10% Pd/C (20 mg). The reaction mixture was stirred under H_2 of 30 psi. at room temperature for 2 hours. Then the reaction mixture was filtered and the filtrate was concentrated to give the crude product (60.0 mg), which was used directly in the next step without further purification. LCMS ($M+H^+$): 350.

Step 3: preparation of tert-butyl (6S)-3-[4-(methanesulfonamidomethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 307c)

A mixture of tert-butyl (6S)-3-[4-(aminomethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **307b**, 20.0 mg, 0.05 mmol), TEA (10.1 mg, 0.1 mmol) and MsCl (9.1 mg, 0.08 mmol) in DCM (5 mL) was stirred at room temperature for 12 hours. The reaction mixture was concentrated to give the crude product (35.0 mg), which was used directly in the next step without further purification. LCMS ($M+H^+$): 428.

Step 4: preparation of tert-butyl (6S)-6-methyl-3-[4-[[methyl(methylsulfonyl)amino]methyl]-2-oxo-pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 307d)

To a solution of tert-butyl (6S)-3-[4-(methanesulfonamidomethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **307c**, 30.0 mg, 0.07 mmol) in DMF (5.0 mL) was added NaH (5.04 mg 0.21 mmol) slowly, and then MeI (15.61 mg, 0.11 mmol). After stirred at room temperature for 12 hours, the reaction mixture was poured into H_2O (30 mL) and EtOAc (30 mL). The organic phase was separated and concentrated in *vacuo* to provide the crude product (31 mg).

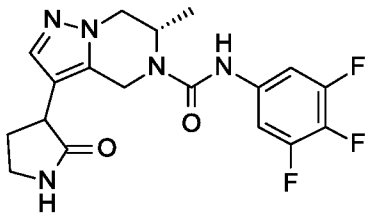
Step 5: preparation of (6S)-6-methyl-3-[4-[[methyl(methylsulfonyl)amino]methyl]-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 307)

The title compound was prepared in analogy to the preparation of Example **11** by using tert-butyl (6S)-6-methyl-3-[4-[[methyl(methylsulfonyl)amino]methyl]-2-oxo-pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **307d**) instead of tert-butyl 3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **11a**). **Example 307** was obtained as a white solid (15 mg). LCMS ($M+H^+$): 515. ^1H NMR (400MHz, DMSO-d_6) δppm 9.14 (br. s., 1H), 7.60 (s, 0.5H), 7.58 (s, 0.5H), 7.51 - 7.32 (m, 2H), 4.97 (d, *J*=17.3 Hz, 1H), 4.84 (d, *J*=5.0 Hz, 1H), 4.36 (dd, *J*=4.0, 17.1 Hz, 1H), 4.24 - 4.17 (m, 1H), 4.15 - 4.09 (m, 1H), 3.92 - 3.78 (m, 1H), 3.57 - 3.48 (m, 1H), 3.25 - 3.15 (m, 1H), 3.07 (dd, *J*=6.8,

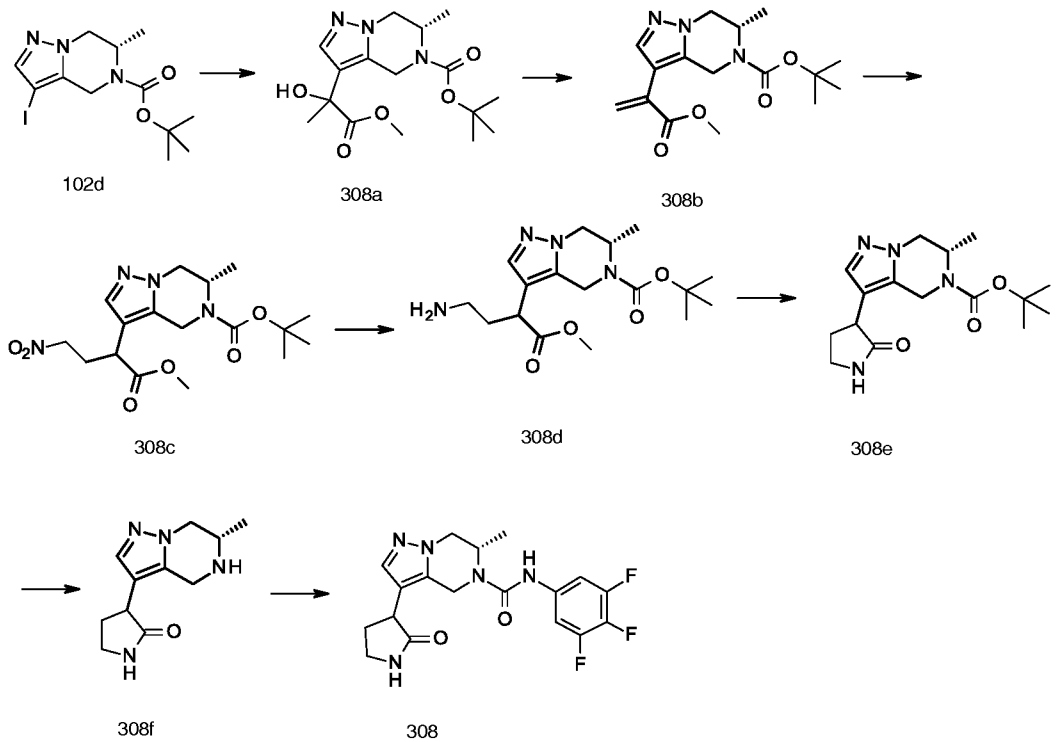
13.3 Hz, 1H), 2.98 - 2.87 (m, 3H), 2.80 (s, 3H), 2.59 (ddd, *J*=3.5, 8.8, 16.8 Hz, 1H), 2.25 - 2.15 (m, 1H), 2.10 - 2.01 (m, 1H), 1.20 - 1.00 (m, 3H).

Example 308:

(6S)-6-methyl-3-(2-oxopyrrolidin-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: Preparation of tert-butyl (6S)-3-(1-hydroxy-2-methoxy-1-methyl-2-oxo-ethyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 308a)

To a solution of tert-butyl (6S)-3-iodo-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **102d**, 500 mg, 1.38 mmol) in THF (10 mL) was added isopropylmagnesium chloride (1.4 mL, 2.76 mmol, 2.0 M in THF) at -10 °C under N_2 atmosphere. The reaction mixture was stirred at 0 °C for 1 hour, then methyl 2-oxopropanoate (281 mg, 2.76 mmol) was added. The resulting mixture was stirred at room temperature for 2

hours, and then quenched with water (10 mL). The resulting mixture was subjected to prep-HPLC to give compound **308a** as a yellow oil (260 mg).

Step 2: Preparation of tert-butyl (6S)-3-(1-methoxycarbonylvinyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 308b)

To a solution of tert-butyl (6S)-3-(1-hydroxy-2-methoxy-1-methyl-2-oxo-ethyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **308a**, 260 mg, 0.77 mmol) and Et_3N (1.55 g, 15.32 mmol) in DCM (8 mL) was added methanesulfonyl chloride (1.66 g, 18.9 mmol) under nitrogen atmosphere. The reaction mixture was stirred at room temperature for 12 hours, and then quenched with water (8 mL). The resulting mixture was purified by prep-HPLC to give compound **308b** as a yellow oil (210 mg).

Step 3: Preparation of tert-butyl (6S)-3-(1-methoxycarbonyl-3-nitro-propyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 308c)

To a solution of tert-butyl (6S)-3-(1-methoxycarbonylvinyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **308b**, 150 mg, 0.47 mmol) in THF (2 mL) was added nitromethane (4 mL) and DBU (7 mg, 0.047 mmol). The reaction mixture was stirred at room temperature for 4 hours, and then purified by prep-HPLC to give compound **308c** as a yellow oil (140 mg).

Step 4: Preparation of tert-butyl (6S)-3-(3-amino-1-methoxycarbonyl-propyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 308d)

To a mixture of tert-butyl (6S)-3-(1-methoxycarbonyl-3-nitro-propyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **308c**, 140 mg, 0.35 mmol) and NH_4Cl (56 mg, 1.06 mmol) in $EtOH/H_2O$ (10 mL/3 mL) was added Fe (79 mg, 1.41 mmol). The reaction mixture was heated at 80 °C with stirring for 4 hrs. After being cooled to room temperature, the reaction mixture was concentrated in *vacuo* to give crude compound **308d**, which was used in the next step without further purification.

Step 5: Preparation of tert-butyl (6S)-6-methyl-3-(2-oxopyrrolidin-3-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 308e)

A suspension of crude tert-butyl (6S)-3-(3-amino-1-methoxycarbonyl-propyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **308d**,124 mg, 0.35 mmol) in toluene (10 mL) was stirred at 100-110 °C for 12 hours. The resulting mixture was concentrated in *vacuo* and the residue was purified by prep-HPLC to give compound **308e** as a yellow oil (14 mg).

Step 6: Preparation of 3-[(6S)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl]pyrrolidin-2-one (compound 308f)

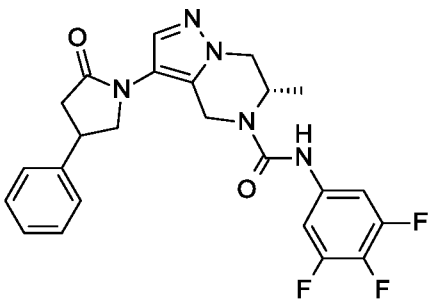
A mixture of tert-butyl (6S)-6-methyl-3-(2-oxopyrrolidin-3-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **308e**, 7 mg, 0.022 mmol) in a solution of HCl in EtOAc (3 mL) was stirred at room temperature for 2 hours. The reaction mixture was concentrated in *vacuo* to give compound **308f** as a yellow oil (5 mg), which was used in the next step without further purification.

Step 7: Preparation of (6S)-6-methyl-3-(2-oxopyrrolidin-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 308)

To a mixture of 3-[(6S)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl]pyrrolidin-2-one (compound **308f**, 5 mg, 0.021 mmol) and phenyl N-(3,4,5-trifluorophenyl)carbamate (6 mg, 0.021 mmol) in DMF (2 mL) was added Et_3N (6 mg, 0.063 mmol). The reaction mixture was stirred at room temperature for 12 hours, and then concentrated in *vacuo*. The residue was purified by prep-HPLC to give **Example 308** as a white solid (5 mg). LCMS ($M+H^+$): 394. ^1H NMR (400 MHz, MeOD) δ ppm 8.53 (br. s., 1H), 7.50 (s, 1H), 7.22 - 7.39 (m, 2H), 5.01 - 5.23 (m, 2H), 4.50 (d, 1H), 4.23 - 4.36 (m, 1H), 4.11 - 4.20 (m, 1H), 3.63 - 3.73 (m, 1H), 3.41 - 3.56 (m, 2H), 2.55 - 2.65 (m, 1H), 2.27 (dt, 1H), 1.17 - 1.34 (m, 3H).

Example 309

(6S)-6-methyl-3-(2-oxo-4-phenyl-pyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



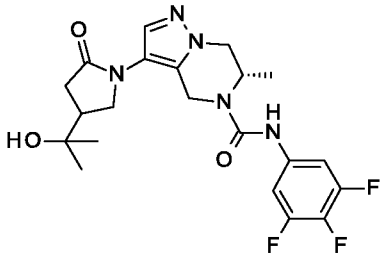
Preparation of (6S)-6-methyl-3-(2-oxo-4-phenyl-pyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 309)

The title compound was prepared in analogy to Example **223** by using 4-phenylpyrrolidin-2-one instead of pyrrolidin-2-one and phenyl N-(3,4,5-trifluoro-phenyl)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). Example **309** (6 mg) was obtained as a white solid. LCMS ($M+H^+$): 470. ^1H NMR (400MHz, MeOD) δ

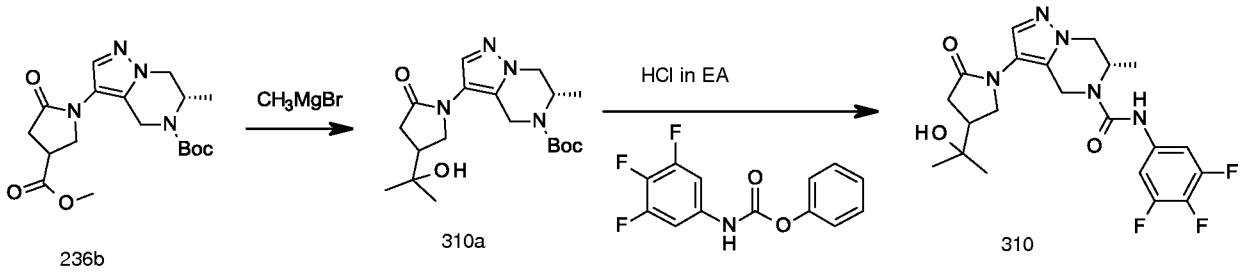
ppm 7.65 (d, *J*=1.1 Hz, 1H), 7.40 - 7.35 (m, 5H), 7.29 - 7.25 (m, 2H), 5.12 - 4.91 (m, 1H), 4.60 (s, 1H), 4.56 - 4.49 (m, 1H), 4.32 - 4.26 (m, 1H), 4.21 - 4.14 (m, 2H), 3.93 - 3.84 (m, 2H), 2.99 - 2.93 (m, 1H), 2.78 - 2.71 (m, 1H), 1.29 - 1.25 (m, 3H).

Example 310

(6S)-3-[4-(1-hydroxy-1-methyl-ethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



236b 310a 310

Step 1: Preparation of tert-butyl (6S)-3-[4-(1-hydroxy-1-methyl-ethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 310a)

To a solution of (6S)-tert-butyl 3-(4-(methoxycarbonyl)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **236b**, 150.0 mg, 0.4 mmol) in THF (20.0 mL) was added a solution of CH_3MgBr (1.4 mL, 4.0 mmol) in THF at 0 °C. The reaction mixture was stirred at room temperature for 5 hours, and then concentrated. The crude product was purified by prep-TLC (PE: EtOAc=1: 1) to give compound **310a** as a colorless oil (100 mg).

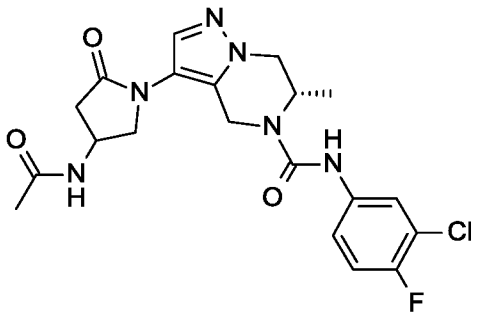
Step 2: Preparation of (6S)-3-[4-(1-hydroxy-1-methyl-ethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 310)

The title compound was prepared in analogy to Example **223** by using tert-butyl (6S)-3-[4-(1-hydroxy-1-methyl-ethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-

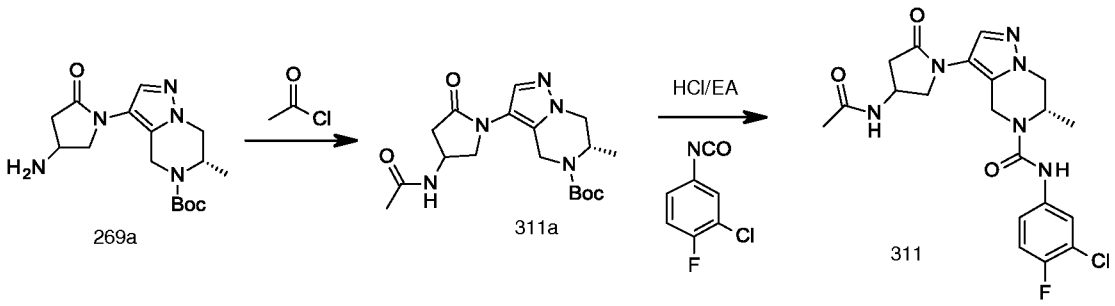
a]pyrazine-5-carboxylate (compound **310a**) instead of tert-butyl (6S)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **223b**) and phenyl N-(3,4,5-trifluoro-phenyl)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 310** was obtained as a yellow solid (8.3 mg). LCMS ($M+H^+$): 452. ^1H NMR (400 MHz, MeOD) δ ppm 7.64 (s, 1H), 7.33-7.26 (m, 2H), 5.05 - 5.00 (m, 1H), 4.98 - 4.95 (m, 1H), 4.49 (dd, *J*=16.94, 9.66 Hz, 1H), 4.33 - 4.26 (m, 1H), 4.16 (d, *J*=12.80 Hz, 1H), 3.89 – 3.79 (m, 2H), 2.73 - 2.65 (m, 1H), 2.63 - 2.49 (m, 2H), 1.28-1.26 (m, 9 H).

Example 311

(6S)-3-(4-acetamido-2-oxo-pyrrolidin-1-yl)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: Preparation of tert-butyl (6S)-3-(4-acetamido-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 311a)

To a solution of (6S)-tert-butyl 3-(4-amino-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **269a**, 100.0 mg, 0.30 mmol) in DCM (5.0 mL) was added Et_3N (60.2 mg, 0.596 mmol) and acetyl chloride (28.1 mg, 0.36 mmol) at 0 °C, then the reaction mixture was stirred at room temperature for 1 hour. The reaction

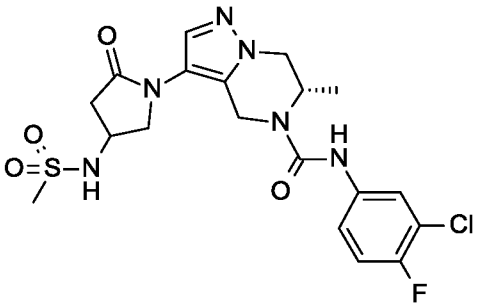
mixture was concentrated to give crude compound **311a** as a yellow solid (100 mg). LCMS: ($M+H^+$): 378.

Step 2: Preparation of (6S)-3-(4-acetamido-2-oxo-pyrrolidin-1-yl)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 311)

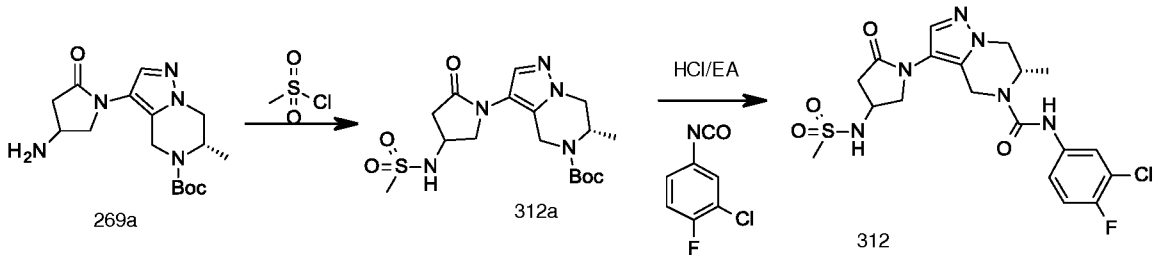
The title compound was prepared in analogy to **Example 246** by using tert-butyl (6S)-3-(4-acetamido-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **311a**) instead of tert-butyl (6S)-3-(3,6-dioxo-4,7,8,8a-tetrahydro-1H-pyrrolo[1,2-a]pyrazin-2-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **246f**). **Example 311** was obtained as a white solid. LCMS: ($M+H^+$): 449. ^{1}H NMR (400MHz, MeOD) δ 7.65 - 7.60 (m, 2H), 7.40 - 7.31 (m, 1H), 7.18 (t, *J*=9.0 Hz, 1H), 5.05 (d, *J*=17.1 Hz, 1H), 4.97 (d, *J*=6.0 Hz, 1H), 4.63 - 4.55 (m, 1H), 4.51 (dd, *J*=3.6, 16.9 Hz, 1H), 4.31 (dd, *J*=4.4, 12.7 Hz, 1H), 4.21 - 4.12 (m, 2H), 3.67 (dt, *J*=3.9, 9.6 Hz, 1H), 2.95 (dd, *J*=8.5, 17.3 Hz, 1H), 2.50 (dd, *J*=4.4, 17.4 Hz, 1H), 2.00 (d, *J*=2.0 Hz, 3H), 1.29-1.27 (m, 3H).

Example 312

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-[4-(methanesulfonamido)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: Preparation of tert-butyl (6S)-3-[4-(methanesulfonamido)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 312a)

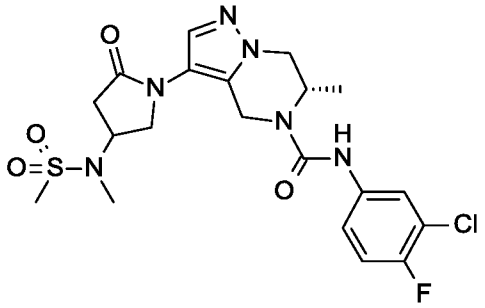
To a solution of (6S)-tert-butyl 3-(4-amino-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **269a**, 100.0 mg, 0.30 mmol) in DCM (5 mL) was added Et_3N (60.2 mg, 0.60 mmol) and methanesulfonyl chloride (41.1 mg, 0.36 mmol) at 0 °C, then the reaction mixture was stirred at room temperature for 1 hour. The reaction mixture was concentrated to give crude compound **312a** as a yellow solid (100 mg). LCMS: ($M+H^+$): 414.

Step 2: Preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-3-[4-(methanesulfonamido)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 312)

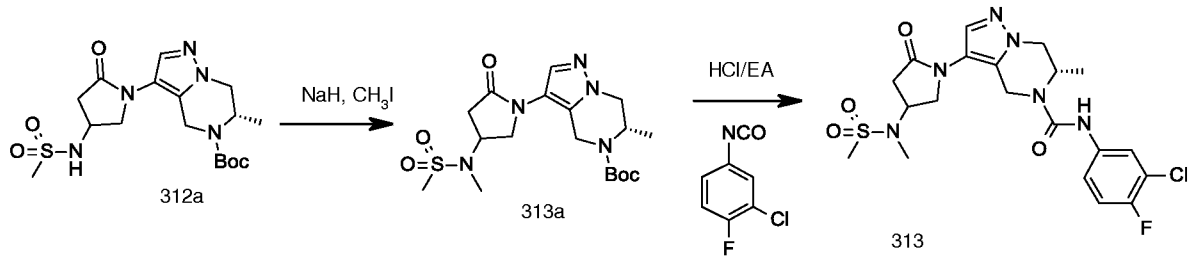
The title compound was prepared in analogy to **Example 246** by using tert-butyl (6S)-3-[4-(methanesulfonamido)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **312a**) instead of tert-butyl (6S)-3-(3,6-dioxo-4,7,8,8a-tetrahydro-1H-pyrrolo[1,2-a]pyrazin-2-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **246f**). **Example 312** was obtained as a white solid (9 mg). LCMS: ($M+H^+$): 485. ^{1}H NMR (400MHz, MeOD) δ 7.68 - 7.58 (m, 2H), 7.34 (td, *J*=3.4, 8.8 Hz, 1H), 7.18 (t, *J*=9.0 Hz, 1H), 5.05 (dd, *J*=3.9, 16.9 Hz, 1H), 4.95 (br. s., 1H), 4.50 (d, *J*=17.1 Hz, 1H), 4.39 - 4.28 (m, 2H), 4.20 - 4.11 (m, 2H), 3.78 (ddd, *J*=4.8, 7.7, 10.2 Hz, 1H), 3.04 (s, 3H), 2.98 (dd, *J*=8.0, 17.3 Hz, 1H), 2.56 (dd, *J*=5.4, 17.2 Hz, 1H), 1.30-1.26 (m, 3H).

Example 313

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-[4-[methyl(methylsulfonyl)amino]-2-oxo-pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: Preparation of tert-butyl (6S)-6-methyl-3-[4-[methyl(methylsulfonyl)amino]-2-oxo-pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 313a)

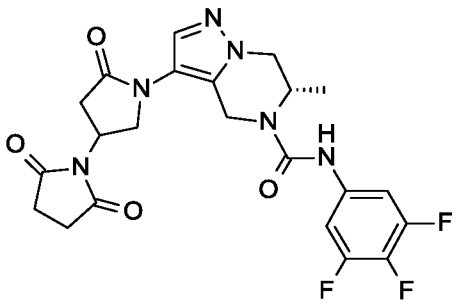
To a solution of tert-butyl (6S)-3-[4-(methanesulfonamido)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **312a**, 60.0 mg, 0.15 mmol) in DCM (5 mL) was added NaH (11.6 mg, 0.29 mmol) and MeI (13.7 mg, 0.17 mmol) at 0 °C, then the reaction mixture was stirred at room temperature for 2 hours. The reaction mixture was poured into ice-water, extracted with DCM. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated to give crude compound **313a** as a yellow oil (40 mg). LCMS: ($M+H^+$): 428.

Step 2: Preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-[4-[methyl(methylsulfonyl)amino]-2-oxo-pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 313)

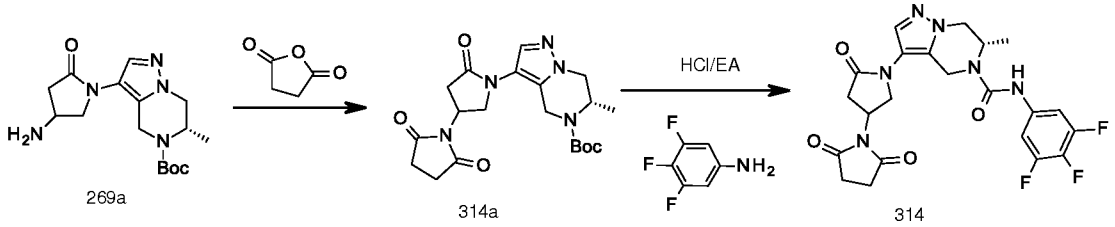
The title compound was prepared in analogy to **Example 246** by using tert-butyl (6S)-6-methyl-3-[4-[methyl(methylsulfonyl)amino]-2-oxo-pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **313a**) instead of tert-butyl (6S)-3-(3,6-dioxo-4,7,8,8a-tetrahydro-1H-pyrrolo[1,2-a]pyrazin-2-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **246f**). **Example 313** was obtained as a white solid (13 mg). LCMS: ($M+H^+$): 499. ^1H NMR (400MHz, MeOD) δ ppm 7.69 (d, *J*=3.3 Hz, 1H), 7.62 (dd, *J*=2.5, 6.5 Hz, 1H), 7.37 - 7.30 (m, 1H), 7.18 (t, *J*=8.9 Hz, 1H), 5.05 (dd, *J*=2.5, 16.8 Hz, 1H), 4.96 (d, *J*=5.5 Hz, 2H), 4.51 (dd, *J*=4.4, 16.9 Hz, 1H), 4.35 - 4.27 (m, 1H), 4.21 - 4.07 (m, 2H), 3.96 - 3.85 (m, 1H), 2.97 (s, 3H), 2.94 (s, 3H), 2.91 - 2.86 (m, 1H), 2.81 - 2.66 (m, 1H), 1.31 - 1.25 (m, 3H).

Example 314

(6S)-3-[4-(2,5-dioxopyrrolidin-1-yl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: Preparation of tert-butyl (6S)-3-[4-(2,5-dioxopyrrolidin-1-yl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 314a)

To a solution of (6S)-tert-butyl 3-(4-amino-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **269a**, 100 mg, 0.29 mmol) in DMF (5 mL) was added tetrahydrofuran-2,5-dione (44.0 mg 0.44 mmol) and DMAP (18.3 mg, 0.15 mmol), then the reaction mixture was stirred at 110°C for 12 hours. The reaction mixture was concentrated in *vacuo* to provide the crude product, which was purified by Prep-HPLC to give compound **314a** as a white solid (50 mg). LCMS: ($M+H^+$): 418.

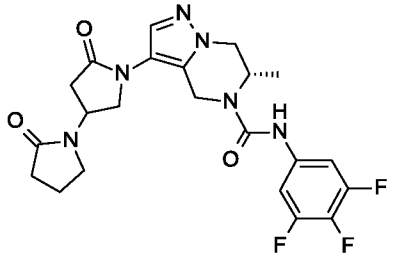
Step 2: Preparation of (6S)-3-[4-(2,5-dioxopyrrolidin-1-yl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 314)

The title compound was prepared in analogy to the preparation of Example **11** by using tert-butyl (6S)-3-[4-(2,5-dioxopyrrolidin-1-yl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **314a**) instead of tert-butyl 3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **11a**).

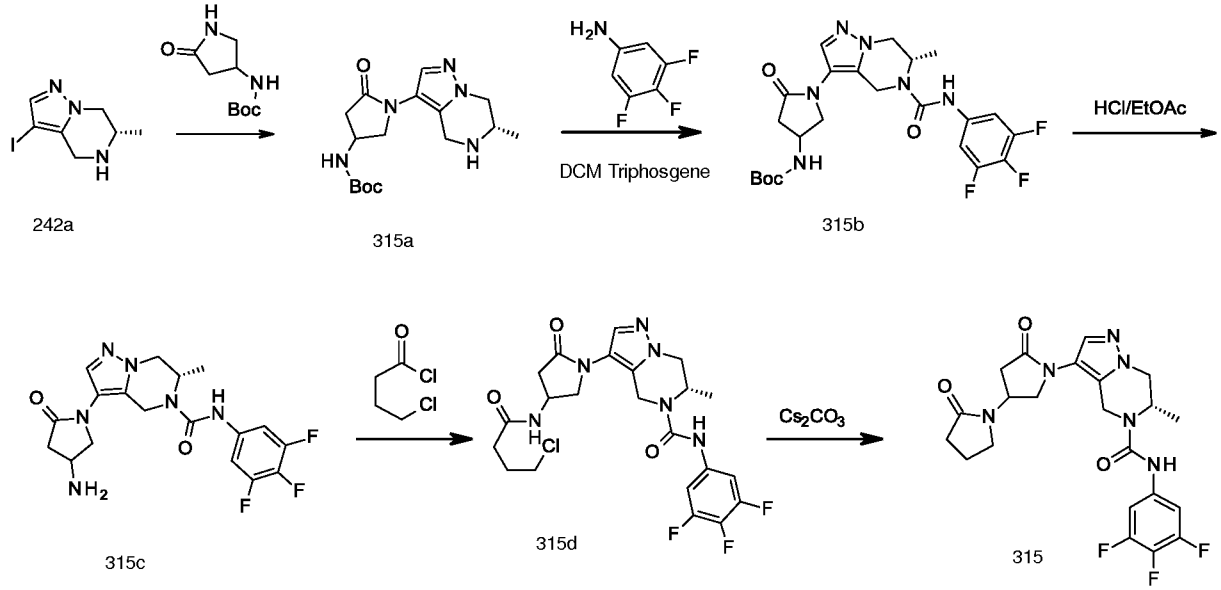
Example 314 was obtained as white solid (15 mg). LCMS ($M+H^+$):491. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 9.20 - 9.14 (m, 1H), 7.57 (d, *J*=4.0 Hz, 1H), 7.43 (dd, *J*=6.5, 10.8 Hz, 2H), 5.10 - 4.98 (m, 1H), 4.95 - 4.77 (m, 2H), 4.42 - 4.31 (m, 1H), 4.27 - 4.18 (m, 1H), 4.16 - 4.00 (m, 2H), 3.83 - 3.68 (m, 1H), 3.66 - 3.47 (m, 1H), 2.87 - 2.74 (m, 1H), 2.65 - 2.59 (m, 3H), 2.42 - 2.31 (m, 1H), 1.19-1.15 (m, 3H).

Example 315

(6S)-6-methyl-3-[2-oxo-4-(2-oxopyrrolidin-1-yl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: preparation of tert-butyl N-[1-[(6S)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl]-5-oxo-pyrrolidin-3-yl]carbamate (compound 315a)

To a solution of tert-butyl N-(5-oxopyrrolidin-3-yl)carbamate (0.88 g, 4.4 mmol) in dioxane (15 mL) was added (6S)-3-iodo-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine(compound **242a**, 1.05 g, 4.0 mmol), (1R,2R)-N1,N2-dimethylcyclohexane-1,2-diamine (57.0 mg, 0.4 mmol), K_3PO_4 (1.7 g, 8.0 mmol) and CuI (76.0 mg, 0.4 mmol) under N_2, and the reaction mixture was stirred at 120 °C for 12 hours. The reaction mixture was filtered and concentrated in *vacuo*, and the residue was purified by silica gel column chromatography (DCM/MeOH=50/1 to 10/1) to give compound **315a** as white solid (800 mg). LCMS ($M+H^+$): 336.

Step 2: preparation of tert-butyl N-[1-[(6S)-6-methyl-5-[(3,4,5-trifluorophenyl)carbamoyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-5-oxo-pyrrolidin-3-yl]carbamate (compound 315b)

To a mixture of 3,4,5-trifluoroaniline (88.82 mg 0.6 mmol) and DIPEA (154.8 mg 1.2 mmol) in DCM (10 mL) was added triphosgene (53.42 mg 0.18 mmol) between 0 °C and 5 °C. The reaction mixture was stirred at room temperature for 1 hour, and then tert-butyl N-[1-[(6S)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl]-5-oxo-pyrrolidin-3-yl]carbamate (compound **315a**, 100.0 mg 0.3 mmol) was added. The resulting mixture was stirred at 30 °C for 12 hours, and then concentrated to afford a residue, which was purified by prep-HPLC to give compound **315b** as white solid (95 mg). LCMS ($M+H^+$): 509.

Step 3: preparation of (6S)-3-(4-amino-2-oxo-pyrrolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (compound 315c)

A solution of tert-butyl N-[1-[(6S)-6-methyl-5-[(3,4,5-trifluorophenyl)carbamoyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-5-oxo-pyrrolidin-3-yl]carbamate (compound **315b**, 95 mg, 0.19 mmol) in HCl/EtOAc (10 mL) was stirred at room temperature for 1 hour. The reaction mixture was concentrated in *vacuo* to give crude compound **315c** (80 mg) which was used directly without further purification. LCMS (M+H+): 409.

Step 4: preparation of (6S)-3-[4-(4-chlorobutanoylamino)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (compound 315d)

To a mixture of (6S)-3-(4-amino-2-oxo-pyrrolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (compound **315c**, 100 mg, 0.24 mmol) and Et_3N (74.2 mg, 0.74 mmol) in DCM (3 mL) at 0 °C was added 4-chlorobutanoyl chloride (41.4 mg, 0.3 mmol). The reaction mixture was stirred at room temperature for 12 hours and concentrated to afford the crude product which was purified by prep-HPLC to give compound **315d** as a white solid (55 mg). LCMS (M+H+): 514.

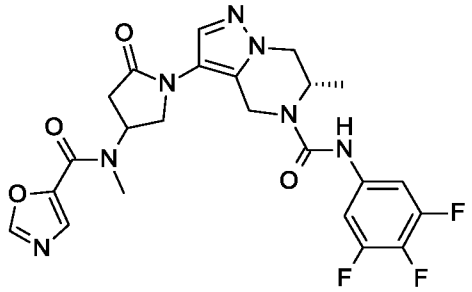
Step 5: preparation of (6S)-6-methyl-3-[2-oxo-4-(2-oxopyrrolidin-1-yl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 315)

A mixture of (6S)-3-[4-(4-chlorobutanoylamino)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (compound **315d**, 45.0 mg, 0.09 mmol) and Cs_2CO_3 (162.9 mg, 0.5 mmol) in DMF (2 mL) was stirred at 80 °C for 12 hours. The reaction mixture was filtered, and the solvents were removed in *vacuo*. The crude product was purified by prep-HPLC to give **Example 315** as yellow solid (15 mg). LCMS ($M+H^+$): 477. ^1H NMR (400 MHz, MeOD) δ ppm 7.67 (s, 0.5H), 7.66 (s, 0.5H), 7.33-7.24 (m, 2 H), 5.12 – 4.97 (m, 3 H), 4.52 (dd, *J*=17.07, 9.29 Hz, 1 H), 4.30 (dd, *J*=12.80, 4.27 Hz, 1 H),

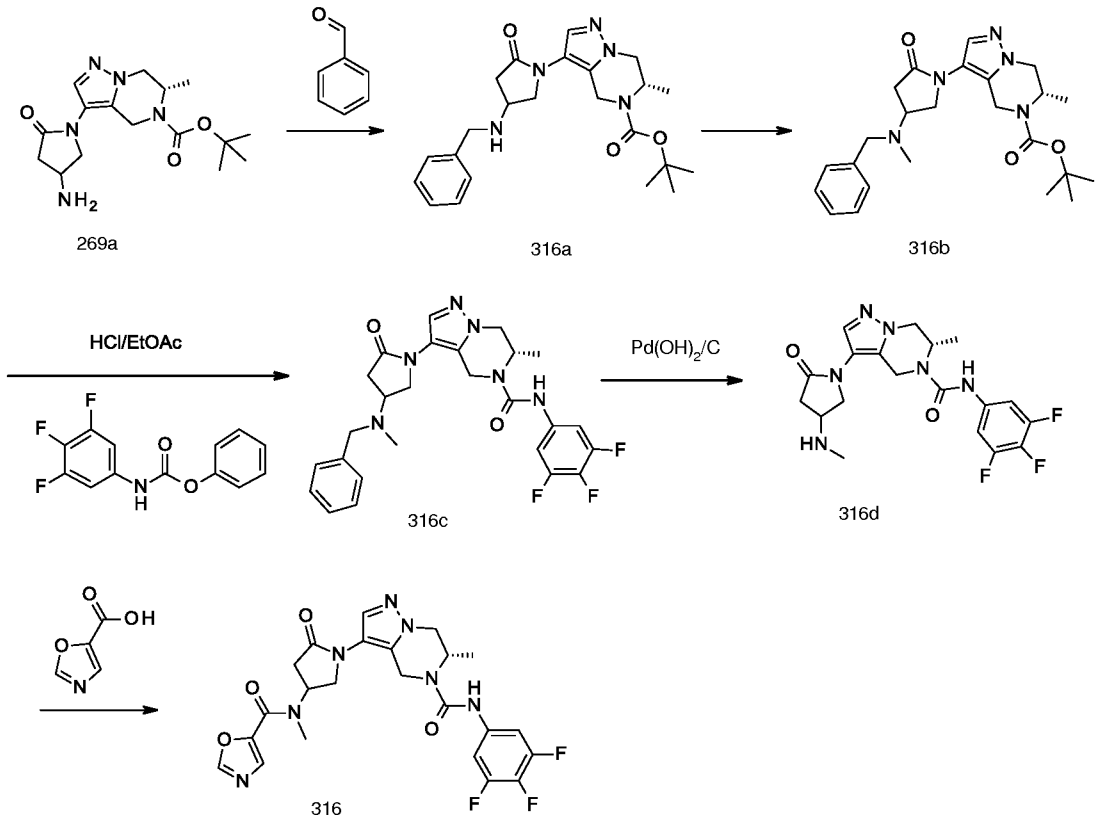
4.21 – 4.09 (m, 2 H), 3.83 (m, *J*=13.36, 10.23, 3.76 Hz, 1 H), 3.56 (t, *J*=7.03 Hz, 2 H), 2.92 (dd, *J*=17.57, 9.03 Hz, 1 H), 2.67 (dd, *J*=17.94, 4.14 Hz, 1 H), 2.44 (td, *J*=8.09, 2.38 Hz, 2 H), 2.17 - 2.08 (m, 2 H), 1.30-1.24 (m, 3H).

Example 316

N-methyl-N-[1-[(6S)-6-methyl-5-[(3,4,5-trifluorophenyl)carbamoyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-5-oxo-pyrrolidin-3-yl]oxazole-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: preparation of tert-butyl (6S)-3-[4-(benzylamino)-2-oxo-pyrrolidin-1-yl]-6 methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 316a)

A mixture of tert-butyl (6S)-3-(4-amino-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **269a**, 1.7 g 5.07 mmol) and benzaldehyde

(0.65 g, 6.08 mmol) in MeOH (10.0 mL) was stirred at room temperature for 1 hour. Then $NaBH_4$ (0.2 g, 5.07 mmol) was added to previous reaction mixture. The resulting reaction mixture was stirred for 12 hours and concentrated in *vacuo* to afford a crude product, which was purified by column chromatography (DCM: MeOH= 10:1) to give compound **316a** as a white solid (2.1 g). LCMS ($M+H^+$): 336

Step 2: preparation of tert-butyl (6S)-3-[4-[benzyl(methyl)amino]-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 316b)

A mixture of tert-butyl (6S)-3-[4-(benzylamino)-2-oxo-pyrrolidin-1-yl]-6 methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **316a**, 2.1 g, 4.9 mmol) and paraformaldehyde (177.0 mg, 5.88 mmol) in CH_3CN (20 mL) was stirred at room temperature for 1 hour. Then $NaBH(OAc)_3$ (1.04 g, 4.9 mmol) was added to previous reaction mixture. The resulting reaction mixture was stirred for another 12 hours, then H_2O (5.0 mL) and EtOAc (50.0 mL) were added, and the organic phase was separated and concentrated to give crude compound **316b** (2.2 g) which was used directly without further purification. LCMS ($M+H^+$): 440.

Step 3: preparation of (6S)-3-[4-[benzyl(methyl)amino]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (compound 316c)

Compound **316c** was prepared in analogy to Example **223** by using tert-butyl (6S)-3-[4-[benzyl(methyl)amino]-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **316b**) instead of tert-butyl (6S)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **223b**), and phenyl N-(3,4,5-trifluorophenyl)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). Compound **316c** was obtained as a light yellow oil (1.8 g). LCMS ($M+H^+$): 513.

Step 4: preparation of (6S)-6-methyl-3-[4-(methylamino)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (compound 316d)

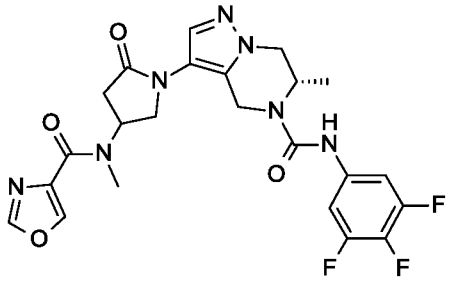
To a solution of (6S)-3-[4-[benzyl(methyl)amino]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (compound **316c**, 302.2 mg, 0.59 mmol) in MeOH (5 mL) was added $Pd(OH)_2/C$ (41.97 mg, 0.3 mmol). The resulting mixture was stirred at room temperature under H_2 at 50 psi for 1 hour. The reaction mixture was filtered and concentrated in *vacuo* to provide crude compound **316d** (160 mg) which was used directly without further purification. LCMS ($M+H^+$): 423.

Step 5: preparation of N-methyl-N-[1-[(6S)-6-methyl-5-[(3,4,5-trifluorophenyl)carbamoyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-5-oxo-pyrrolidin-3-yl]oxazole-5-carboxamide (Example 316)

A mixture of oxazole-5-carboxylic acid (11.3 mg, 0.10 mmol), DIPEA (56.8 mg, 0.44 mmol), EDCI (38.5 mg, 0.33 mmol) and HOBT (26.4 mg, 0.33 mmol) in DMF (1.0 mL) was stirred for 30 mins before the addition of (6S)-6-methyl-3-[4-(methylamino)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (compound **316d**, 50.0 mg, 0.11 mmol) in DMF (5 mL). The reaction mixture was stirred at 30 °C for 12 hours. The reaction mixture was filtered and concentrated to afford the residue which was purified by prep-HPLC to give Example **316** as a white solid (10 mg). LCMS ($M+H^+$): 518. ^1H NMR(400 MHz, DMSO-d6) δ ppm 9.20 (s, 0.5H), 9.18 (s, 0.5H), 8.59 (s, 1H), 7.78 (br. s., 1H), 7.71 - 7.61 (m, 1H), 7.49-7.41 (m, 2H), 5.26 (br. s., 1H), 5.10 – 4.98 (m, 1H), 4.87 (br. s., 1H), 4.40 (d, *J*=17.07 Hz, 1H), 4.26 - 4.18 (m, 1H), 4.17- 4.00 (m, 2H), 3.93 - 3.76 (m, 1H), 3.16 (br. s., 2H),2.94 - 2.65 (m, 3H), 1.19-1.13 (m, 3H).

Example 317

N-methyl-N-[1-[(6S)-6-methyl-5-[(3,4,5-trifluorophenyl)carbamoyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-5-oxo-pyrrolidin-3-yl]oxazole-4-carboxamide

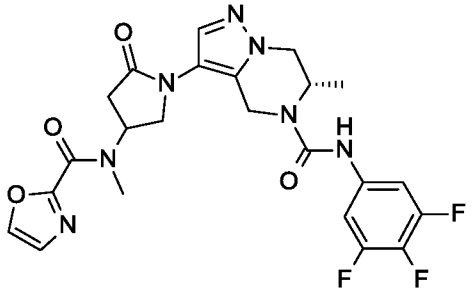


Preparation of Example 317

The title compound was prepared in analogy to Example **316** by using oxazole-4-carboxylic acid instead of oxazole-5-carboxylic acid. Example **317** was obtained as a white solid (9.4 mg). LCMS ($M+H^+$): 518.1. ^1H NMR (400 MHz, DMSO-d6) δ ppm 9.27 (s, 0.5H), 9.25 (s, 0.5H),, 8.62 (s, 1H), 8.54 (br. s., 1H), 7.66 (d, *J*=5.27 Hz, 1H), 7.50-7.43 (m, 2H), 5.49 - 5.26 (m, 1H), 5.06 (dd, *J*=17.32, 7.78 Hz, 1H), 4.89 (br. s., 1H), 4.39 (d, *J*=17.32 Hz, 1H), 4.26 - 4.17 (m, 1H), 4.16 – 3.98 (m, 2H), 3.84 (br. s., 1H), 3.22 (br. s., 2H), 2.97 - 2.65 (m, 3H), 1.19-1.13 (m, 3H).

Example 318

N-methyl-N-[1-[(6S)-6-methyl-5-[(3,4,5-trifluorophenyl)carbamoyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-5-oxo-pyrrolidin-3-yl]oxazole-2-carboxamide

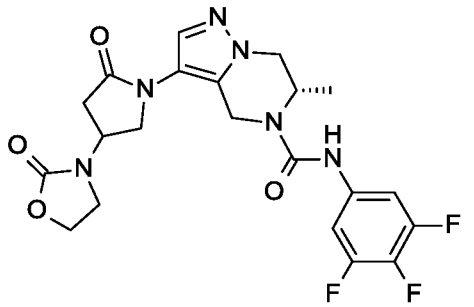


Preparation of Example 318

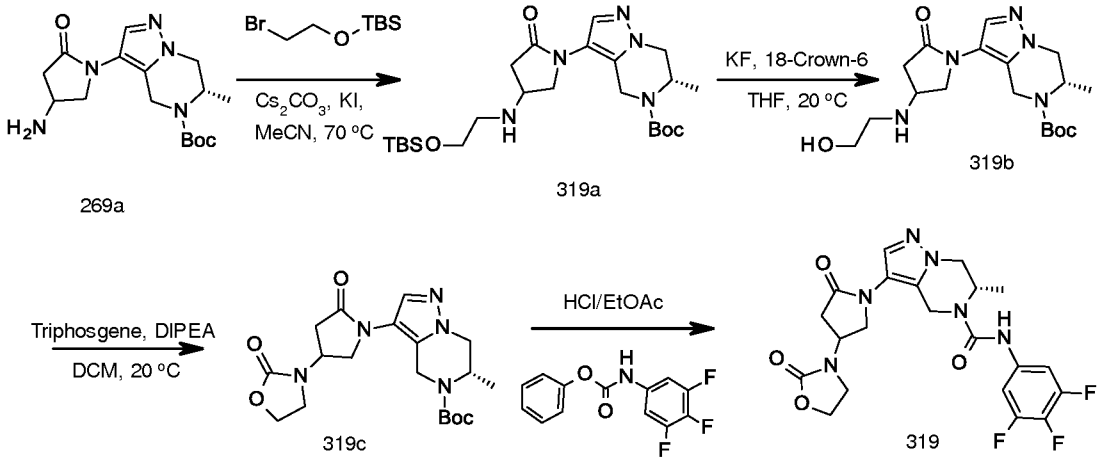
The title compound was prepared in analogy to Example **316** by using oxazole-2-carboxylic acid instead of oxazole-5-carboxylic acid. Example **318** was obtained as a white solid (6.2 mg). LCMS ($M+H^+$): 518. ^1H NMR (400 MHz, MeOH) δ ppm 8.14 - 8.06 (m, 1H), 7.73 - 7.65 (m, 1H), 7.41 (s, 1H), 7.33-7.27 (m, 2H), 5.10 - 5.05 (m, 1H), 4.97 (br. s., 1H), 4.64 - 4.49 (m, 2H), 4.36 - 4.22 (m, 2H), 4.20 - 4.13 (m, 1H), 4.07 – 3.89 (m, 1H), 3.51 (s, 2H), 3.17 (s, 1H), 3.08 – 2.96 (m, 1H), 2.89 - 2.78 (m, 1H), 1.30-1.26 (m, 3H).

Example 319

(6S)-6-methyl-3-[2-oxo-4-(2-oxooxazolidin-3-yl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: preparation of (6S)-tert-butyl 3-(4-(2-(tert-butyldimethylsilyloxy)ethylamino)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 319a)

A mixture of tert-butyl (6S)-3-(4-amino-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **269a**, 400.0 mg, 1.19 mmol), (2-bromoethoxy)(tert-butyl)dimethylsilane (313.8 mg, 1.31 mmol), Cs_2CO_3 (777.1 mg, 2.39 mmol) and KI (39.6 mg, 0.34mmol) in MeCN (5.0 mL) was stirred at 70 °C for 12 hours. The reaction mixture was concentrated and the residue was purified by prep-TLC to give compound **319a** as a yellow oil (100 mg).

Step 2: preparation of (6S)-tert-butyl 3-(4-(2-hydroxyethylamino)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 319b)

To a solution of (6S)-tert-butyl 3-(4-(2-(tert-butyldimethylsilyloxy)ethylamino)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **319a**, 100.0 mg, 0.20 mmol) in THF (5 mL) was added KF (81.9 mg, 1.41 mmol) and 18-Crown-6 (372.7 mg, 1.41 mmol), and the reaction mixture was stirred at room temperature for 16 hours. The reaction mixture was concentrated and the residue was purified by prep-TLC (DCM:MeOH=10:1, Rf=0.25) to give compound **319b** as a yellow oil (32 mg).

Step 3: preparation of (6S)-tert-butyl 6-methyl-3-(2-oxo-4-(2-oxooxazolidin-3-yl)pyrrolidin-1-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 319c)

To a solution of (6S)-tert-butyl 3-(4-(2-hydroxyethylamino)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **319b**, 22.0 mg, 0.06 mmol) in DCM (2 mL) was added DIPEA (22.5 mg, 0.17 mmol) and triphosgene (9.0 mg, 0.03 mmol), and the reaction mixture was stirred at room temperature for 15 hours. The reaction

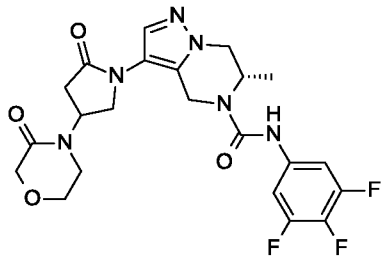
mixture was concentrated and the residue was purified by prep-TLC (DCM:MeOH=10:1) to afford compound **319c** as yellow oil (11 mg).

Step 4: (6S)-6-methyl-3-[2-oxo-4-(2-oxooxazolidin-3-yl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 319)

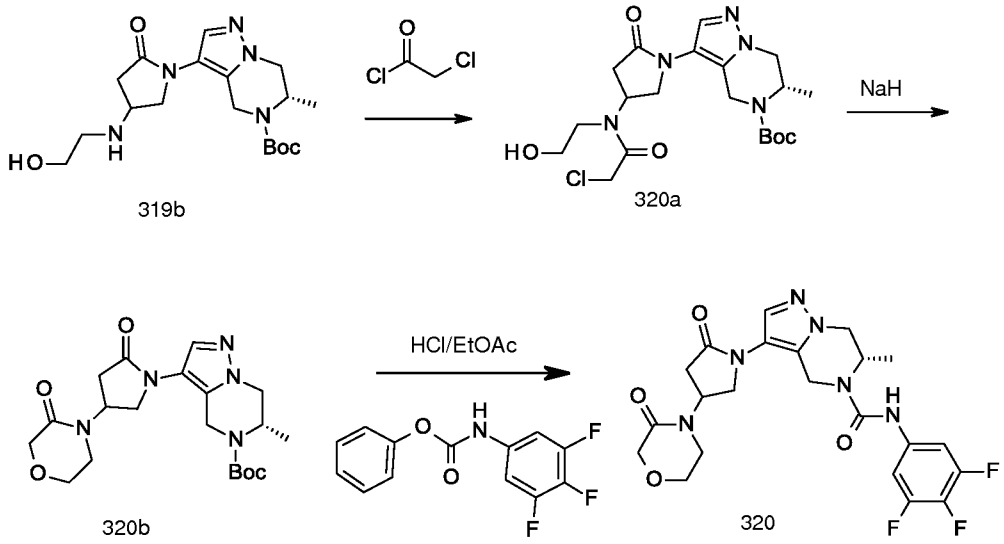
The title compound was prepared in analogy to Example **223** by using (6S)-tert-butyl 6-methyl-3-(2-oxo-4-(2-oxooxazolidin-3-yl)pyrrolidin-1-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **319c**) instead of tert-butyl (6S)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **223b**) and phenyl N-(3,4,5-trifluoro-phenyl)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). Example **319** was obtained as a white solid (5.9 mg). LCMS: ($M+H^+$): 479. ^{1}H NMR(400MHz, MeOD) δ ppm 7.69 - 7.63 (m, 1H), 7.34 - 7.22 (m, 2H), 5.11 - 5.01 (m, 1H), 5.00 - 4.90 (m, 1H), 4.74 - 4.64 (m, 1H), 4.56 - 4.46 (m, 1H), 4.46 - 4.38 (m, 2H), 4.34 - 4.26 (m, 1H), 4.18 (s, 2H), 3.97 - 3.85 (m, 1H), 3.75 (d, *J*=8.8 Hz, 2H), 3.03 - 2.86 (m, 1H), 2.78 - 2.69 (m, 1H), 1.32 - 1.24 (m, 3H).

Example 320

(6S)-6-methyl-3-[2-oxo-4-(3-oxomorpholin-4-yl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: preparation of (6S)-tert-butyl 3-(4-(2-chloro-N-(2-hydroxyethyl)acetamido)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 320a)

To a mixture of (6S)-tert-butyl 3-(4-(2-hydroxyethylamino)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **319b**, 100.0 mg, 0.26 mmol) and Et_3N (29.3 mg 0.29 mmol) in DCM (5.0 mL) was added 2-chloroacetyl chloride (29.1 mg, 0.26 mmol) dropwise. The reaction mixture was stirred at room temperature for 12 hours, and then concentrated. The residue was purified by Prep-HPLC to give compound **320a** as a yellow oil (50 mg). LCMS: ($M+H^+$): 456.

Step 2: preparation of (6S)-tert-butyl 6-methyl-3-(2-oxo-4-(3-oxomorpholino)pyrrolidin-1-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 320b)

To a solution of (6S)-tert-butyl 3-(4-(2-chloro-N-(2-hydroxyethyl)acetamido)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **320a**, 50.0 mg, 0.11 mmol) in THF (5.0 mL) was added NaH (8.8 mg, 0.22 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 1 hour, quenched with H_2O (20 mL) and extracted with EtOAc (20 mL) twice. The combined organic layer was concentrated to provide crude compound **320b** as a colorless oil (20 mg). LCMS: ($M+H^+$): 420.

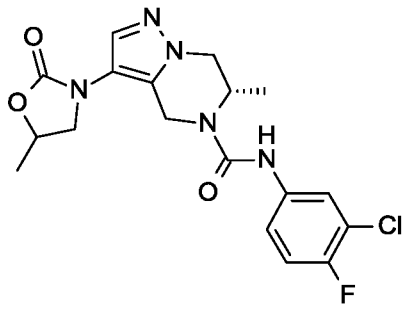
Step 3: preparation of (6S)-6-methyl-3-[2-oxo-4-(3-oxomorpholin-4-yl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 320)

The title compound was prepared in analogy to Example **223** by using (6S)-tert-butyl 6-methyl-3-(2-oxo-4-(3-oxomorpholino)pyrrolidin-1-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-

5(4H)-carboxylate (compound **320b**) instead of tert-butyl (6S)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **223b**) and phenyl N-(3,4,5-trifluoro-phenyl)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). Example **320** was obtained as white solid (10.5 mg). LCMS: ($M+H^+$): 493. ^{1}H NMR (400MHz, DMSO-d_6) δ ppm 8.45 (br. s., 1H), 7.66 (s, 0.5H), 7.64 (s, 0.5H), 7.36-7.50 (m, 2H), 5.23 (br. s., 1H), 4.99 (dd, *J*=17.1, 3.5 Hz, 1H), 4.86 (br. s., 1H), 4.38 (dd, *J*=17.2, 3.6 Hz, 1H), 3.94-4.25 (m, 5H), 3.68-3.91 (m, 3H), 2.77 (dd, *J*=17.4, 9.4 Hz, 1H), 2.60 (d, *J*=4.0 Hz, 1H), 2.53-2.57 (m, 2H), 1.15 (d, *J*=6.8 Hz, 3H).

Example 321

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(5-methyl-2-oxo-oxazolidin-3-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

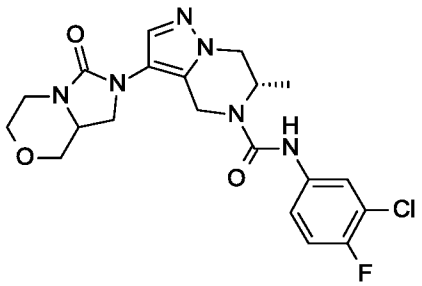


Preparation of Example 321

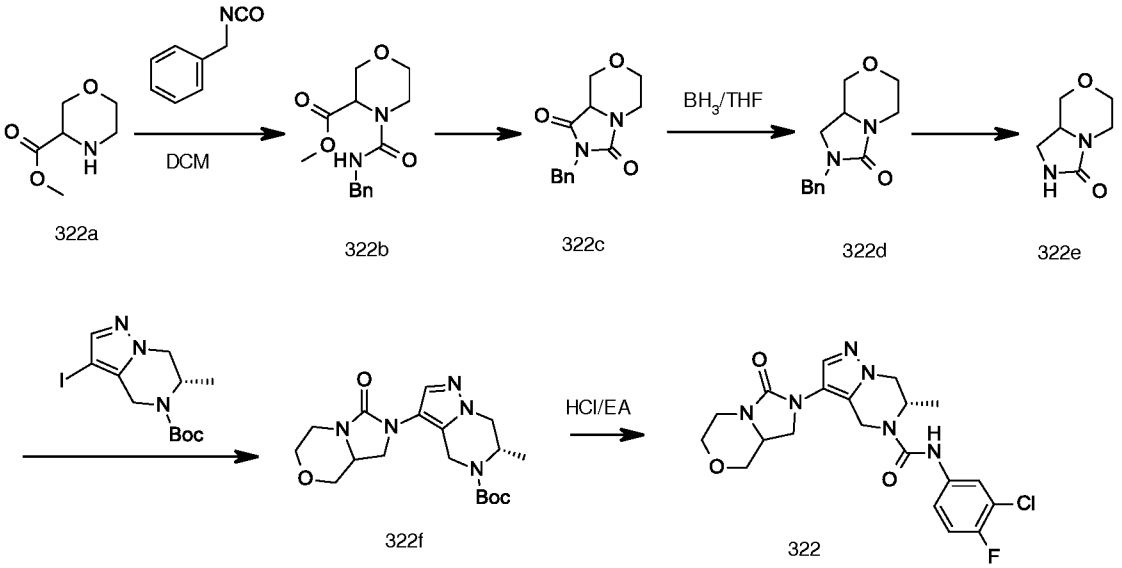
The title compound was prepared in analogy to Example **246** by using5-methyloxazolidin-2-one instead of 1,2,4,7,8,8a-hexahydropyrrolo[1,2-a]pyrazine-3,6-dione (compound **246e**). Example **321**was obtained as a white solid (47.6 mg). LCMS ($M+H^+$):408.^{1}H NMR (400MHz, DMSO-d_6) δppm 8.95 (s, 1H), 7.74 (dd, *J*=2.5, 6.8 Hz, 1H), 7.61 (s, 1H), 7.48 - 7.39 (m, 1H), 7.37 - 7.28 (m, 1H), 5.02 (dd, *J*=4.9, 16.9 Hz, 1H), 4.93 - 4.85 (m, 1H), 4.85 - 4.77 (m, 1H), 4.39 (dd, *J*=4.5, 17.1 Hz, 1H), 4.25 - 4.17 (m, 1H), 4.15 - 4.08 (m, 1H), 4.08 - 4.00 (m, 1H), 3.65 - 3.52 (m, 1H), 1.47 - 1.39 (m, 3H), 1.18 - 1.08 (m, 3H).

Example 322

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(3-oxo-5,6,8,8a-tetrahydro-1H-imidazo[5,1-c][1,4]oxazin-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



322a 322b 322c 322d 322e

322f 322

Step 1: preparation of methyl 4-(benzylcarbamoyl)morpholine-3-carboxylate (compound 322b)

To a solution of methyl morpholine-3-carboxylate (compound **322a,** 300.0 mg, 2.06 mmol) in DCM (3 mL) was added (isocyanatomethyl)benzene (275.2 mg, 2.06 mmol). The reaction mixture was stirred at room temperature for 2 hours, then washed with brine, dried over Na_2SO_4, and concentrated to give crude compound **322b** (500 mg) as a colourless oil, which was used in next step directly. LCMS:($M+H^+$): 279.

Step 2: preparation of 2-benzyl-tetrahydro-2H-imidazo[5,1-c][1,4]oxazine-1,3-dione (compound 322c)

A solution of methyl 4-(benzylcarbamoyl)morpholine-3-carboxylate (compound **322b**, 500 mg, 1.80 mmol) in EtOH (6 mL) was stirred at 90 °C for 12 hours, and then concentrated. The residue was purified by silica gel column chromatography (PE/EtOAc=5/1) to give compound **322c** as colorless oil (450 mg). LCMS: ($M+H^+$): 247

Step 3: preparation of 2-benzyl-hexahydroimidazo[5,1-c][1,4]oxazin-3-one (compound 322d)

To a solution of 2-benzyl-tetrahydro-2H-imidazo[5,1-c][1,4]oxazine-1,3-dione (compound **322c**, 350.0 mg, 1.42 mmol) in THF (2 mL) was added BH_3/THF (14.2 mL, 14.2 mmol) at 0 °C and the reaction mixture was stirred at 80 °C for 12 hours, then MeOH was added and the reaction mixture was concentrated to afford the residue which was purified by silica gel column chromatography (PE/EtOAc=3/1) to give compound **322d** as colorless oil (300 mg). LCMS: ($M+H^+$): 233.

Step 4: preparation of hexahydroimidazo[5,1-c][1,4]oxazin-3-one (compound 322e)

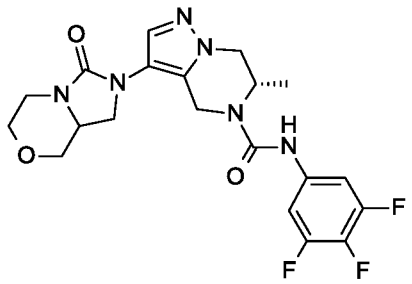
To a solution of 2-benzyl-hexahydroimidazo[5,1-c][1,4]oxazin-3-one (compound **322d,** 300.0 mg, 1.29 mmol) in THF (3.0 mL) at -78 °C was added liquid ammonia (10 mL), then EtOH (1 mL) and Na (150.0 mg). The resulting dark blue mixture was stirred for 30 mins at -78 °C and quenched with solid NH_4Cl. After warmed to room temperature, the reaction mixture was taken up in EtOAc (10 mL) and washed with water (5 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by Prep-HPLC to give compound **322e** as a white solid. ^1H NMR(400MHz, MeOD) δ ppm 3.91 - 3.78 (m, 3H), 3.63 (dd, *J*=2.8, 13.6 Hz, 1H), 3.51 (t, *J*=8.9 Hz, 1H), 3.44 - 3.37 (m, 1H), 3.13 - 3.03 (m, 1H), 3.00 (dd, *J*=4.5, 9.5 Hz, 1H).

reparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(3-oxo-5,6,8,8a-tetrahydro-1H-imidazo[5,1-c][1,4]oxazin-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 322)

The title compound was prepared in analogy to Example **246** by using hexahydroimidazo[5,1-c][1,4]oxazin-3-one (compound **322e**) instead of 1,2,4,7,8,8a-hexahydropyrrolo[1,2-a]pyrazine-3,6-dione (compound **246e**). Example **322** was obtained as white solid (4.7 mg). LCMS: ($M+H^+$): 449. ^1H NMR (400MHz, DMSO-d_6) δ ppm 8.95 (d, *J*=3.6 Hz, 1H), 7.74 (dd, *J*=2.6, 6.8 Hz, 1H), 7.54 (d, *J*=2.1 Hz, 1H), 7.47 - 7.40 (m, 1H), 7.36 - 7.28 (m, 1H), 5.00 (dd, *J*=13.2, 16.8 Hz, 1H), 4.86 (d, *J*=5.0 Hz, 1H), 4.40 (dd, *J*=9.9, 16.9 Hz, 1H), 4.23 - 4.14 (m, 1H), 4.13 - 4.06 (m, 1H), 3.93 - 3.71 (m, 4H), 3.61 - 3.55 (m, 1H), 3.31 (br. s., 3H), 3.08 - 3.00 (m, 1H), 1.17-1.10 (m, 3H).

Example 323

(6S)-6-methyl-3-(3-oxo-5,6,8,8a-tetrahydro-1H-imidazo[5,1-c][1,4]oxazin-2-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

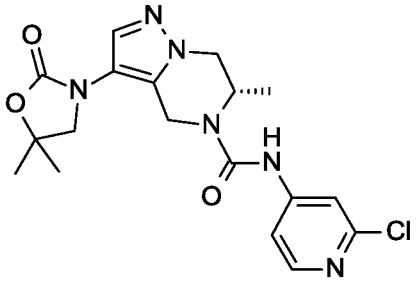


Preparation of Example 323

The title compound was prepared in analogy to Example **223** by using hexahydroimidazo[5,1-c][1,4]oxazin-3-one (compound **322e**) instead of pyrrolidin-2-one and phenyl (3,4,5-trifluorophenyl)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). Example **323** was obtained as a white solid (22.5mg). LCMS: 451. ^{1}H NMR(400MHz, DMSO-d_6) δ ppm 9.10 (d, *J*=5.8 Hz, 1H), 7.54 (d, *J*=2.0 Hz, 1H), 7.43 (ddd, *J*=2.3, 6.6, 10.6 Hz, 2H), 5.06 - 4.93 (m, 1H), 4.91 - 4.76 (m, 1H), 4.41 (dd, *J*=12.6, 16.9 Hz, 1H), 4.25 - 4.15 (m, 1H), 4.14 - 4.06 (m, 1H), 3.94 - 3.70 (m, 4H), 3.57 (dd, *J*=2.6, 13.4 Hz, 1H), 3.33 - 3.25 (m, 3H), 3.04 (dt, *J*=3.8, 12.6 Hz, 1H), 1.17-1.10 (m, 3H).

Example 324

(6S)-N-(2-chloro-4-pyridyl)-3-(5,5-dimethyl-2-oxo-oxazolidin-3-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

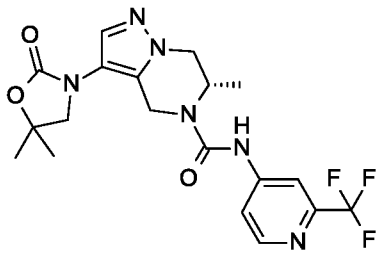


Preparation of Example 324

The title compound was prepared in analogy to Example **223** by using 5,5-dimethyloxazolidin-2-one instead of pyrrolidin-2-one and phenyl N-(2-chloro-4-pyridyl)carbamate instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). Example **324** was obtained as a white solid (5.6 mg). LCMS (M+H$^+$): 405.^{1}H NMR(400 MHz, MeOD) δ ppm8.45 (d, *J*=6.02 Hz, 1H), 8.19 (s, 1H), 7.95 (d, *J*=5.52 Hz, 1H), 7.70 (s, 1H), 5.26 (d, *J*=16.81 Hz, 1H), 5.07 (br. s., 1H), 4.65 (d, *J*=16.31 Hz, 1H), 4.36 (d, *J*=9.79 Hz, 1H), 4.20 (d, *J*=12.55 Hz, 1H), 3.86 (br. s., 2H), 1.58 (s, 6H), 1.32 (d, *J*=6.53 Hz, 3H)

Example 325

(6S)-3-(5,5-dimethyl-2-oxo-oxazolidin-3-yl)-6-methyl-N-[2-(trifluoromethyl)-4-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

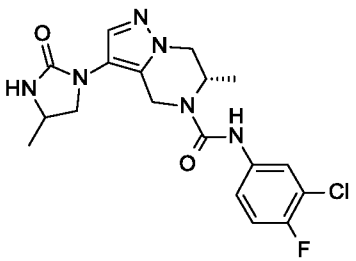


Preparation of Example 325

The title compound was prepared in analogy to Example **223** by using 5,5-dimethyloxazolidin-2-one instead of pyrrolidin-2-one and phenyl N-(2-trifluoromethyl-4-pyridyl)carbamate instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). Example **325** was obtained as a white solid (15 mg).LCMS ($M+H^+$): 439.^{1}H NMR(400 MHz, MeOD)δppm 8.71 (d, *J*=6.53 Hz, 1H), 8.55 (d, *J*=5.27 Hz, 1H), 8.25 - 8.33 (m, 1H), 7.84 - 7.93 (m, 1H), 5.39 (dd, *J*=17.19, 8.41Hz, 1H), 5.22 (br. s., 1H), 4.71 (d, *J*=17.07 Hz, 1H), 4.39 - 4.49 (m, 1H), 4.26 (d, *J*=12.80 Hz, 1H), 3.86 - 3.95 (m, 2H), 1.59 (s, 6H), 1.35 (d, *J*=6.78 Hz, 3H).

Example 326

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(4-methyl-2-oxo-imidazolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



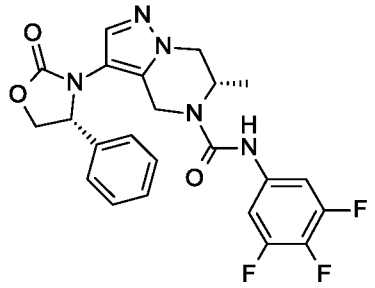
Preparation of Example 326

The title compound was prepared in analogy to Example **246** by using 4-methylimidazolidin-2-one instead of 1,2,4,7,8,8a-hexahydropyrrolo[1,2-a]pyrazine-3,6-dione (compound **246e**). Example **326** was obtained as a white solid(15 mg). LCMS: ($M+H^+$): 407. ^{1}H NMR(400MHz, MeOD) δ ppm 7.63 (dd, *J*=2.5, 6.5 Hz, 1H), 7.57 (s, 1H), 7.35 (td, *J*=4.2, 7.2 Hz, 1H), 7.18 (t, *J*=8.9 Hz, 1H), 5.06 (dd, *J*=3.9, 16.7 Hz, 1H), 4.97 (d, *J*=5.5 Hz, 1H), 4.54 (dd,

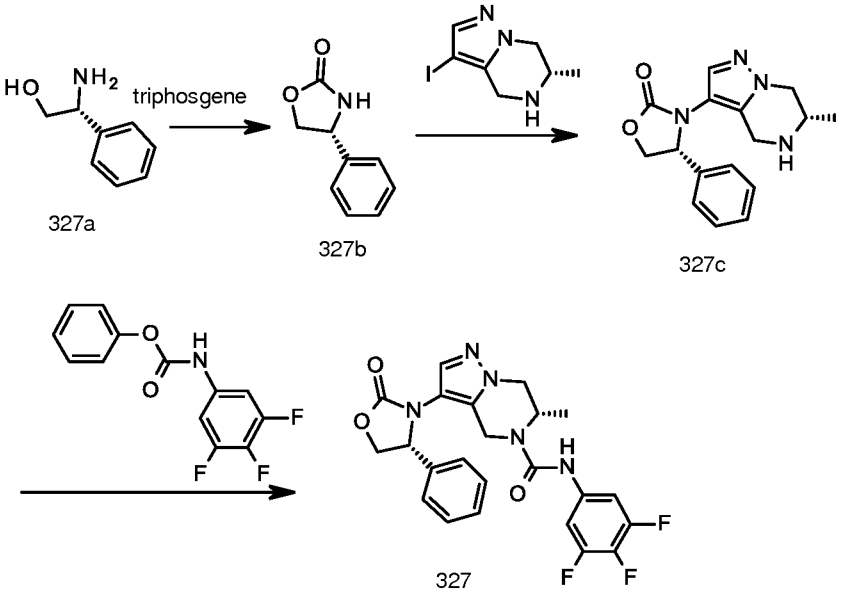
J=3.9, 16.7 Hz, 1H), 4.29 (d, *J*=12.8 Hz, 1H), 4.14 (d, *J*=12.8 Hz, 1H), 4.02 - 3.92 (m, 2H), 3.46 (br. s., 1H), 1.34 (d, *J*=5.5 Hz, 3H), 1.29-1.22 (m, 3H).

Example 327

(6S)-6-methyl-3-[(4R)-2-oxo-4-phenyl-oxazolidin-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: Preparation of (4R)-4-phenyloxazolidin-2-one (compound 327b)

To a solution of (2R)-2-amino-2-phenyl-ethanol (274.4 mg, 2.0 mmol) in DCM (3 mL) was added Et_3N (607.1 mg, 6.0 mmol) and triphosgene (77.8 mg, 0.6 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 12 hours, then concentrated in *vacuo* to give crude product, which was purified by prep-HPLC to give compound **327b** as a white solid (130 mg). LCMS($M+H^+$): 164.

Step 2: Preparation of (4R)-3-[(6S)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl]-4-phenyl-oxazolidin-2-one (compound 327c)

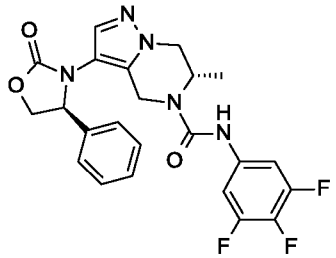
To a solution of (4R)-4-phenyloxazolidin-2-one (compound **327b**, 67.7 mg, 0.42) in dioxane (15 mL) was added (6S)-3-iodo-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine(compound **242a**, 100.0 mg, 0.38 mmol), (1R,2R)-N1,N2-dimethylcyclohexane-1,2-diamine (21.3 mg, 0.15 mmol), K_3PO_4 (161.9 mg, 0.76 mmol) and CuI (28.5 mg, 0.15 mmol) under N_2, and the reaction mixture was stirred at 120 °C for 12 hours, then filtered and concentrated in *vacuo*, and the residue was purified by prep-HPLC to give compound **327c** as colorless oil (20 mg). LCMS ($M+H^+$): 299.

Step 3: Preparation of (6S)-6-methyl-3-[(4R)-2-oxo-4-phenyl-oxazolidin-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 327)

To a solution of (4R)-3-[(6S)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl]-4-phenyl-oxazolidin-2-one (compound **327c,** 20.0 mg, 0.067 mg) and DIPEA (17.3 mg, 0.134 mmol) in DMF (2 mL) was added phenyl (3,4,5-trifluorophenyl)carbamate (compound **233c**, 19.7 mg, 0.074 mmol) at room temperature and the reaction mixture was stirred at room temperature for 2 hours. The reaction mixture was then purified by prep-HPLC to afford Example **327** as white solid (7.5 mg). LCMS ($M+H^+$): 472. ^{1}H NMR (400MHz, MeOD) δ ppm 7.45 - 7.25 (m, 8H), 5.44 - 5.29 (m, 1H), 4.94 - 4.92 (m, 2H), 4.84 - 4.74 (m, 1H), 4.56 - 4.48 (m, 1H), 4.45 - 4.36 (m, 1H), 4.24 - 4.15 (m, 1H), 4.09 - 4.00 (m, 1H), 1.19 (d, *J*=6.9 Hz, 3H)

Example 328

(6S)-6-methyl-3-[(4S)-2-oxo-4-phenyl-oxazolidin-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

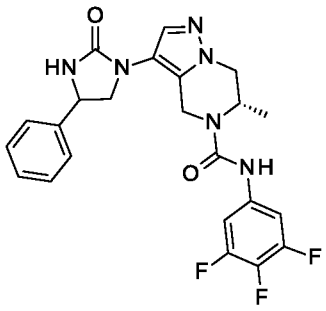


Preparation of Example 328

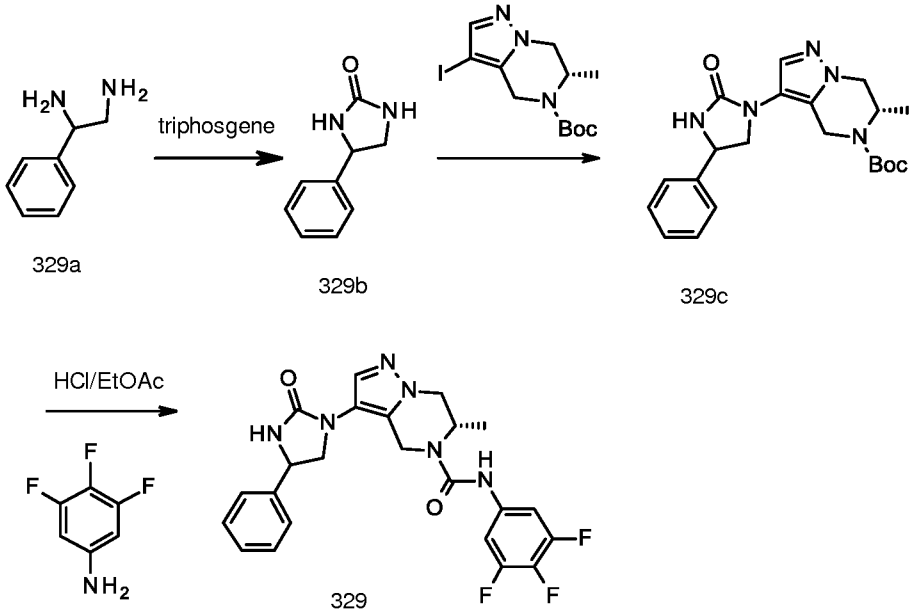
The title compound was prepared in analogy to Example **327** by using (2S)-2-amino-2-phenyl-ethanol instead of (2R)-2-amino-2-phenyl-ethanol (compound **327a**). Example **328** was obtained as a white solid (12 mg). LCMS ($M+H^+$): 472. ^{1}H NMR (400MHz, MeOD) δ ppm 7.50 - 7.22 (m, 8H), 5.31 (dd, *J*=6.7, 8.8 Hz, 1H), 5.04 - 4.90 (m, 3H), 4.55 - 4.44 (m, 1H), 4.21 (dd, *J*=4.2, 12.9 Hz, 1H), 4.12 - 3.97 (m, 2H), 0.94 (d, *J*=6.9 H z, 3H).

Example 329

(6S)-6-methyl-3-(2-oxo-4-phenyl-imidazolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



329a 329b 329c 329

Step 1: preparation of 4-phenylimidazolidin-2-one (compound 329b)

To a solution of 1-phenylethane-1,2-diamine (compound **329a**, 300.0 mg 1.44 mmol) in THF (5 mL) was added DIPEA (557.3 mg, 4.32 mmol) and triphosgene (213.66 mg 0.72 mmol) while keeping inner temperature below 0 °C. The reaction mixture was stirred at 30 °C for 12 hours, and then concentrated. The residue was purified by prep-HPLC to give compound **329b** as a white solid (30 mg). LCMS: ($M+H^+$): 163

Step 2: preparation of (6S)-tert-butyl 6-methyl-3-(2-oxo-4-phenylimidazolidin-1-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 329c)

To a solution of 4-phenylimidazolidin-2-one (compound **329b**, 47.2 mg, 0.13 mmol) in dioxane (5 mL) was added (1R,2R)-N1,N2-dimethylcyclohexane-1,2-diamine (2.84 mg, 0.02 mmol), (6S)-tert-butyl 3-iodo-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate

(compound **102d**, 30.0 mg, 0.19 mmol), K_3PO_4 (54.93mg, 0.26 mmol) and CuI (3.8 mg, 0.02 mmol) under N_2 at room temperature, and the reaction mixture was stirred at 110 °C for 12 hours. Then the reaction mixture was concentrated and the crude product was purified by prep-TLC to provide compund **329c** as a green oil (70 mg) which was used directly without further purification. LCMS: ($M+H^+$): 398.

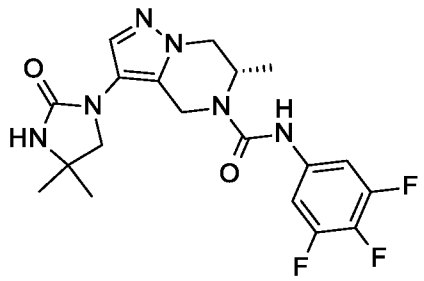
Step 3: preparation of (6S)-6-methyl-3-(2-oxo-4-phenyl-imidazolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 329)

A solution of (6S)-tert-butyl 6-methyl-3-(2-oxo-4-phenylimidazolidin-1-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **329c**, 70.0 mg, 0.18 mmol) in HCl/EtOAc (5.0 mL) was stirred at room temperature for 12 hours, and then concentrated to give a crude product (60 mg) which was used directly without further purification.

To a mixture of 3,4,5-trifluoroaniline (52.9 mg 0.36 mmol) and DIPEA (92.9 mg, 0.72 mmol) in DCM (10.0 mL) was added triphosgene (32.65 mg 0.11 mmol) at 0 °C. After 1 hour to the reaction mixture was added above obtained crude product (60.0 mg 0.18 mmol), and the resulting mixture was stirred at room temperature for 12 hours. Then the reaction mixture was concentrated and the residue was purified by prep-HPLC to give Example **329** as a white solid (12.3 mg). LCMS: ($M+H^+$): 471. ^{1}H NMR (400MHz, $CDCl_3$) δ ppm 8.19 (s, 1H), 7.54 - 7.36 (m, 7H), 7.34 - 7.30 (m, 2H), 5.22 - 5.18 (m, 1H), 5.01 (d, *J*=4.8 Hz, 1H), 4.44 - 4.39 (m, 1H), 4.31 - 4.26 (m, 1H), 4.13 (t, *J*=8.9 Hz, 1H), 4.03 - 3.98 (m, 1H), 3.84 (t, *J*=8.7 Hz, 1H), 3.69 (dd, *J*=6.1, 8.9 Hz, 1H), 1.43 - 1.39 (m, 3H)

Example 330

(6S)-3-(4,4-dimethyl-2-oxo-imidazolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



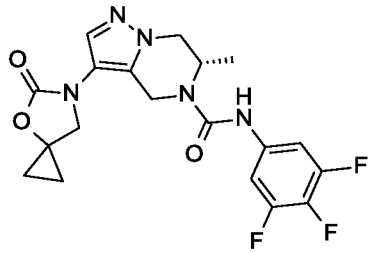
Preparation of (6S)-3-(4,4-dimethyl-2-oxo-imidazolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 330)

The title compound was prepared in analogy to Example **329** by using 2-methylpropane-1,2-diamine instead of 1-phenylethane-1,2-diamine (compound **329a**). Example **330** was

obtained as a white solid (5 mg). LCMS: ($M+H^+$): 423. ^{1}H NMR(400 MHz, DMSO-d_6) δ ppm 9.17 (s, 1H), 8.46 (br. s., 1H), 7.50 (s, 1H), 7.43 (dd, *J*=6.4, 10.9 Hz, 2H), 5.00 (d, *J*=17.1 Hz, 1H), 4.85 (d, *J*=4.8 Hz, 1H), 4.42 (d, *J*=17.1 Hz, 1H), 4.20 - 4.14 (m, 1H), 4.12 - 4.05 (m, 1H), 3.52 (s, 1H), 3.48 (br. s., 1H), 2.10 - 2.04 (m, 3H), 1.28 (s, 3H), 1.14 (d, *J*=6.8 Hz, 3H).

Example 331

(6S)-6-methyl-3-(5-oxo-4-oxa-6-azaspiro[2.4]heptan-6-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

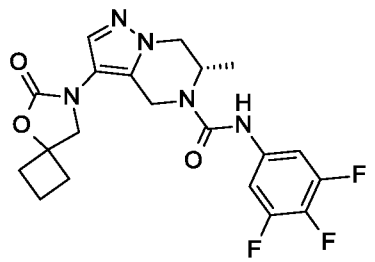


Preparation of (6S)-6-methyl-3-(5-oxo-4-oxa-6-azaspiro[2.4]heptan-6-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 331)

The title compound was prepared in analogy to Example **329** by using 1-(aminomethyl)cyclopropanol instead of 1-phenylethane-1,2-diamine (compound **329a**). Example **331** (24 mg) was obtained as white solid. LCMS: ($M+H^+$): 422. ^{1}H NMR(400 MHz, MeOD) δ ppm 7.66 (s, 1H), 7.28 (dd, *J*=6.3, 10.2 Hz, 2H), 5.08 (d, *J*=16.9 Hz, 1H), 5.02 - 4.93 (m, 1H), 4.54 (d, *J*=16.9 Hz, 1H), 4.32 - 4.25 (m, 1H), 4.17 - 4.08 (m, 3H), 1.26-1.21 (m, 5H), 0.94 - 0.86 (m, 2H).

Example 332

(6S)-6-methyl-3-(6-oxo-5-oxa-7-azaspiro[3.4]octan-7-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

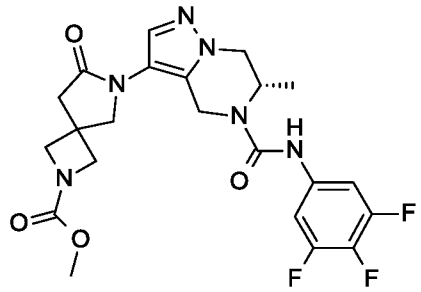


Preparation of (6S)-6-methyl-3-(6-oxo-5-oxa-7-azaspiro[3.4]octan-7-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 332)

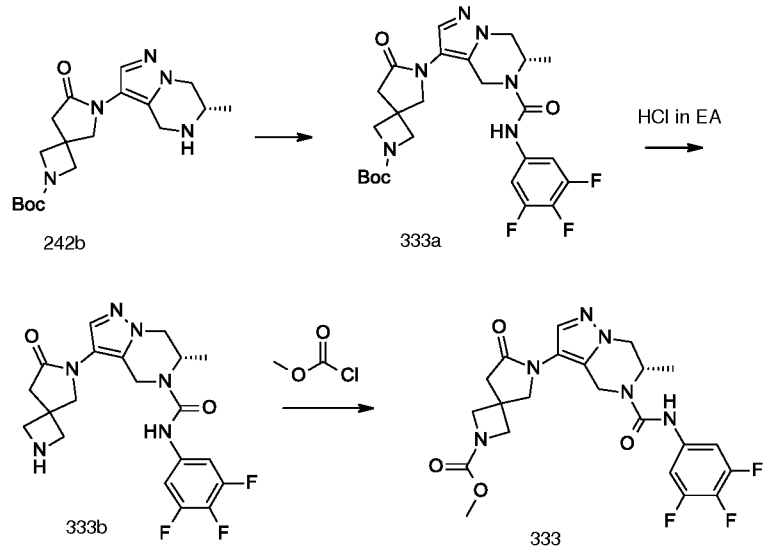
The title compound was prepared in analogy to Example **329** by using 1-(aminomethyl)cyclobutanol instead of 1-phenylethane-1,2-diamine (compound **329a**). Example **332** (15.0 mg) was obtained as white solid. LCMS: ($M+H^+$): 437. ^1H NMR(400 MHz, MeOD) δ ppm 7.64 (s, 1H), 7.33 - 7.23 (m, 2H), 5.06 (d, *J*=16.8 Hz, 1H), 5.01 - 4.94 (m, 1H), 4.53 (d, *J*=16.8 Hz, 1H), 4.29 (dd, *J*=4.3, 12.8 Hz, 1H), 4.19 - 4.06 (m, 3H), 2.64 - 2.52 (m, 2H), 2.39 (m, *J*=3.8, 8.4, 12.4 Hz, 2H), 2.00 - 1.88 (m, 1H), 1.83 - 1.68 (m, 1H), 1.26 (d, *J*=7.0 Hz, 3H).

Example 333

methyl 6-[(6S)-6-methyl-5-[(3,4,5-trifluorophenyl)carbamoyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-7-oxo-2,6-diazaspiro[3.4]octane-2-carboxylate



The title compound was prepared according to the following scheme:



Step 1: preparation of tert-butyl 6-[(6S)-6-methyl-5-[(3,4,5-trifluorophenyl)carbamoyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-7-oxo-2,6-diazaspiro[3.4]octane-2-carboxylate (compound 333a)

A mixture of 3,4,5-trifluoroaniline (244.0 mg, 1.66 mmol), DIPEA (428 mg, 3.32 mmol) and triphosgene (148 mg 0.5 mmol) in DCM (10 mL) was stirred at 0°C for 1 hour, to which was added tert-butyl 6-[(6S)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl]-7-oxo-2,6-

diazaspiro[3.4]octane-2-carboxylate (compound **242b**, 300.0 mg 0.83 mmol). The resulting mixture was stirred at room temperature for 12 hours, and was concentrated. The residue was purified by prep-HPLC to give compound **333a** (60.0 mg) as a white solid. LCMS ($M+H^+$): 535

Step 2: preparation of (6S)-6-methyl-3-(7-oxo-2,6-diazaspiro[3.4]octan-6-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (compound 333b)

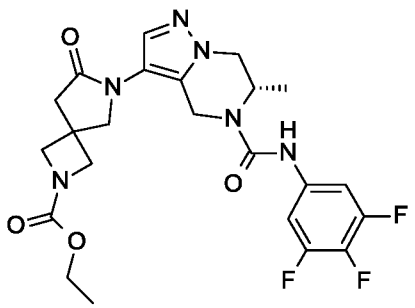
A solution of tert-butyl 6-[(6S)-6-methyl-5-[(3,4,5-trifluorophenyl)carbamoyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-7-oxo-2,6-diazaspiro[3.4]octane-2-carboxylate (compound **333a**, 60 mg, 0.11 mmol) in HCl/EtOAc (10 mL) was stirred at room temperature for 1 hour, and then was concentrated to provide crude compound **333b** (60 mg).

Step 3: preparation of methyl 6-[(6S)-6-methyl-5-[(3,4,5-trifluorophenyl)carbamoyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-7-oxo-2,6-diazaspiro[3.4]octane-2-carboxylate (Example 333)

To a solution of (6S)-6-methyl-3-(7-oxo-2,6-diazaspiro[3.4]octan-6-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (compound **333b**, 20 mg) in DCM (5 mL) was added Et_3N (10 mg) and methyl carbonochloridate (6 mg). The reaction mixture was stirred at 25°C for 1 hour, and then concentrated in *vacuo*. The obtained residue was purified by prep-HPLC to give Example **333** (16 mg) as a white solid. LCMS (M+1): 493. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.12 (s, 1H), 7.60 (s, 1H), 7.45-7.39 (m, 2H), 4.96 (d, *J*=17.1 Hz, 1H), 4.88 - 4.79 (m, 1H), 4.38 (d, *J*=17.3 Hz, 1H), 4.24 - 4.16 (m, 1H), 4.15 - 4.08 (m, 1H), 4.02 - 3.93 (m, 5H), 3.57 (s, 3H), 2.77 (s, 2H), 2.08 (s, 1H), 1.14 (d, *J*=6.8 Hz, 3H).

Example 334

ethyl 6-[(6S)-6-methyl-5-[(3,4,5-trifluorophenyl)carbamoyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-7-oxo-2,6-diazaspiro[3.4]octane-2-carboxylate



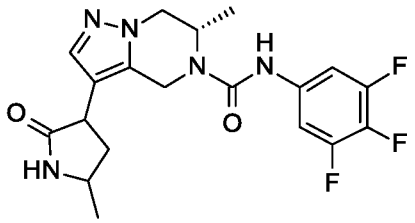
Preparation of Example 334

The title compound was prepared in analogy to Example **333** by using ethyl carbonochloridate instead of methyl carbonochloridate. Example **334** (16 mg) was obtained as a

white solid. LCMS: ($M+H^+$): 507. ^1H NMR (400MHz, DMSO-d_6) δ ppm 9.12 (s, 1H), 7.61 (s, 1H), 7.45-7.39 (m, 2H), 4.96 (d, *J*=17.1 Hz, 1H), 4.90 - 4.80 (m, 1H), 4.38 (d, *J*=17.1 Hz, 1H), 4.23 - 4.16 (m, 1H), 4.15 - 4.08 (m, 1H), 4.04 - 3.90 (m, 7H), 2.76 (s, 2H), 2.08 (s, 1H), 1.24 - 1.08 (m, 6H).

Example 335

(6S)-6-methyl-3-(5-methyl-2-oxo-pyrrolidin-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

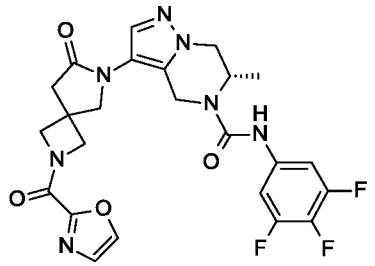


Preparation of Example 335

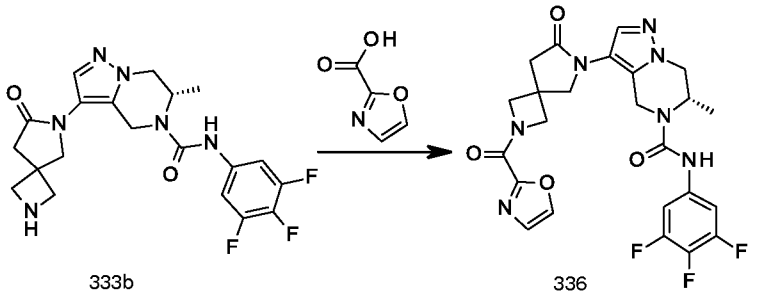
The title compound was prepared in analogy to Example **308** by using nitroethane instead of nitromethane. Example **335** (5 mg) was obtained as a white solid. LCMS ($M+H^+$): 408. ^1H NMR (400 MHz, MeOD) δ ppm 7.45 - 7.55 (m, 1H), 7.20 - 7.37 (m, 2H), 4.96 - 5.19 (m, 2H), 4.43 - 4.58 (m, 1H), 4.25 - 4.32 (m, 1H), 4.09 - 4.19 (m, 1H), 3.72 - 3.97 (m, 2H), 1.77 - 2.70 (m, 2H), 1.13 - 1.36 (m, 6H).

Example 336

(6S)-6-methyl-3-[2-(oxazole-2-carbonyl)-7-oxo-2,6-diazaspiro[3.4]octan-6-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



Preparation of Example 336

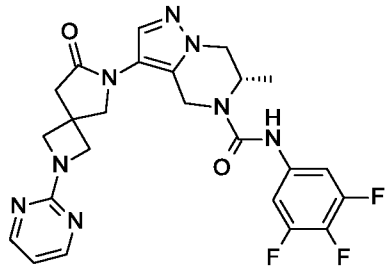


333b 336

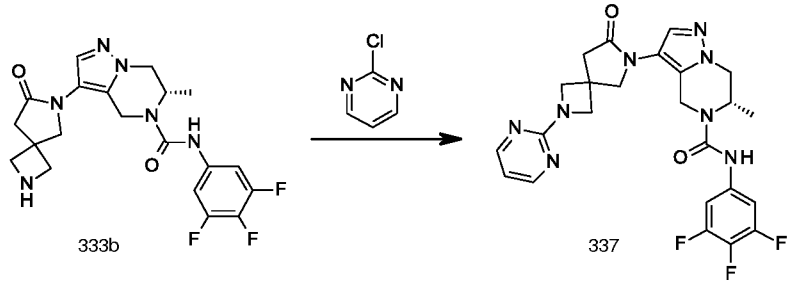
A mixture of (6S)-6-methyl-3-(7-oxo-2,6-diazaspiro[3.4]octan-6-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (compound **333b**, 120.0 mg, 0.28 mmol), oxazole-2-carboxylic acid (35.1 mg, 0.31 mmol), DIPEA (144.5 mg, 1.14 mmol), EDCI (98.0 mg, 0.84 mmol) and HOBt (113.5 mg, 0.84 mmol) in DMF (5 mL) was stirred at 30 °C for 12 hours, and then concentrated in *vacuo*. The crude product was purified by prep-HPLC to give Example **336** (6.7 mg) as a white solid. LCMS ($M+H^+$): 530. ^1H NMR (400 MHz, MeOD) δ ppm 8.10 (s, 1H), 7.66 (s, 1H), 7.40 (s, 1H), 7.33-7.26 (m, 2H), 5.03 (s, 1H), 4.99 - 4.94 (m, 1H), 4.83 - 4.75 (m, 2H), 4.52 (d, *J*=17.1 Hz, 1H), 4.35 - 4.27 (m, 3H), 4.19 - 4.10 (m, 3H), 2.97 (s, 2H), 1.28 (d, *J*=6.8 Hz, 3H).

Example 337

(6S)-6-methyl-3-(7-oxo-2-pyrimidin-2-yl-2,6-diazaspiro[3.4]octan-6-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



Preparation of Example 337



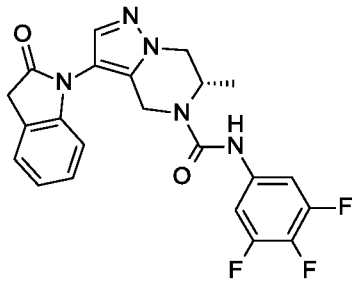
333b 337

A mixture of (6S)-6-methyl-3-(7-oxo-2,6-diazaspiro[3.4]octan-6-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (compound **333b**, 120.0 mg, 0.28 mmol), 2-chloropyrimidine (42.0 mg, 0.36 mmol), Cs_2CO_3 (81.6 mg, 0.6 mmol),

$Pd(dba)_2$ (55.2 mg, 0.06 mmol), Xantphos (CAS:161265-03-8, 34.8 mg, 0.06mmol) in dioxane (5 mL) was stirred at 90 °C in microwave and under N_2 for 2 hours. The reaction mixture was concentrated and the residue was purified by prep-HPLC to give Example **337** as a yellow solid (5.6 mg). LCMS ($M+H^+$): 513. ^1H NMR (400 MHz, MeOD) δ ppm 8.37 (d, *J*=5.0 Hz, 2H), 7.67 (s, 1H), 7.33 - 7.25 (m, 2H), 6.74 (t, *J*=4.9 Hz, 1H), 5.05 (d, *J*=16.8 Hz, 1H), 4.98 (d, *J*=5.3 Hz, 1H), 4.62 (s, 2H), 4.54 (d, *J*=16.8 Hz, 1H), 4.33 - 4.23 (m, 3H), 4.21 - 4.13 (m, 3H), 2.95 (s, 2H), 1.28 (d, *J*=7.0 Hz, 3H).

Example 338

(6S)-6-methyl-3-(2-oxoindolin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

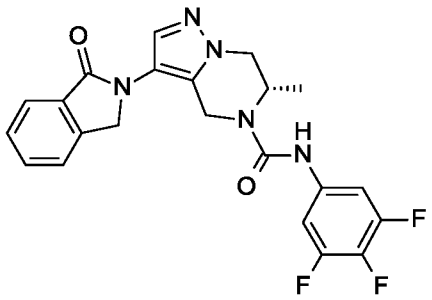


Preparation of Example 338

The title compound was prepared in analogy to Example **223** by using indolin-2-one instead of pyrrolidin-2-one and phenyl N-[3,4,5-trifluoro-phenyl]carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). Example **338** was obtained as a grey solid (38 mg). LCMS ($M+H^+$): 442. ^1H NMR (400MHz, MeOD) δ ppm 7.73 (s, 1H), 7.36 (d, *J*=7.4 Hz, 1H), 7.28 - 7.21 (m, 3H), 7.13 - 7.08 (m, 1H), 6.82 (d, *J*=7.9 Hz, 1H), 5.04 - 4.98 (m, 1H), 4.96 - 4.91 (m, 1H), 4.44 - 4.33 (m, 2H), 4.26 - 4.20 (m, 1H), 3.74 (s, 2H), 1.29 (d, *J*=6.9 Hz, 3H).

Example 339

(6S)-6-methyl-3-(1-oxoisoindolin-2-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

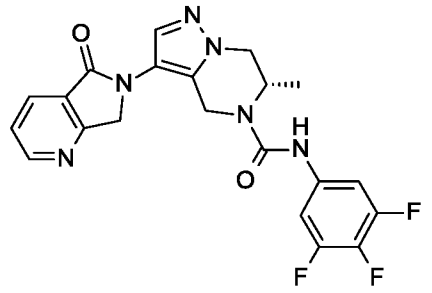


Preparation of Example 339

The title compound was prepared in analogy to Example **223** by using isoindolin-1-one instead of pyrrolidin-2-one and phenyl N-[3,4,5-trifluoro-phenyl]carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). Example **339** was obtained as a grey solid (200 mg). LCMS ($M+H^+$): 442. ^{1}H NMR (400MHz, MeOD) δ ppm 7.82 (d, *J*=7.7 Hz, 1H), 7.77 (s, 1H), 7.63 (s, 2H), 7.54 (s, 1H), 7.29-7.21 (m, 2H), 5.12 (d, *J*=16.8 Hz, 1H), 4.99 (br. s., 1H), 4.89 (d, *J*=10.3 Hz, 2H), 4.61 (d, *J*=16.9 Hz, 1H), 4.33 - 4.26 (m, 1H), 4.21 - 4.15 (m, 1H), 1.28 (d, *J*=6.9 Hz, 3H).

Example 340

(6S)-6-methyl-3-(5-oxo-7H-pyrrolo[3,4-b]pyridin-6-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

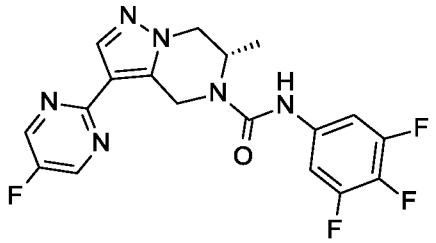


Preparation of Example 340

The title compound was prepared in analogy to Example **223** by using 6,7-dihydropyrrolo[3,4-b]pyridin-5-one instead of pyrrolidin-2-one and phenyl N-[3,4,5-trifluoro-phenyl]carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). Example **340** was obtained as a grey solid (90 mg). LCMS ($M+H^+$): 443. ^{1}H NMR (400MHz, MeOD) δ ppm 8.80 (dd, *J*=1.4, 5.0 Hz, 1H), 8.24 (dd, *J*=1.4, 7.7 Hz, 1H), 7.82 (s, 1H), 7.61 (dd, *J*=5.0, 7.8 Hz, 1H), 7.29-7.22 (m, 2H),, 5.14 (d, *J*=16.9 Hz, 1H), 4.98 (d, *J*=8.8 Hz, 3H), 4.61 (d, *J*=16.9 Hz, 1H), 4.35 - 4.29 (m, 1H), 4.23 - 4.17 (m, 1H), 1.30 (d, *J*=6.9 Hz, 3H).

Example 341

(6S)-3-(5-fluoropyrimidin-2-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

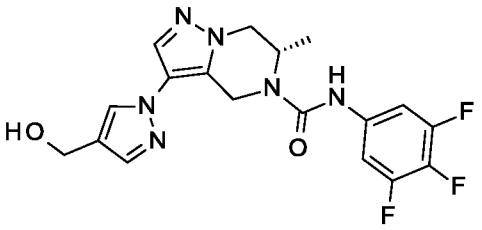


Preparation of Example 341

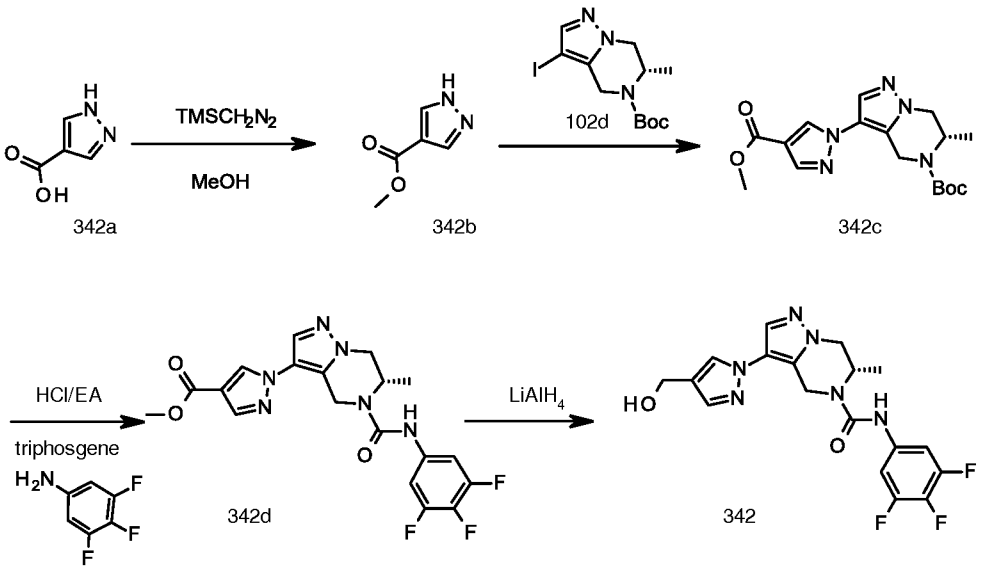
The title compound was prepared in analogy to Example **223** by using tert-butyl (6S)-3-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **288b**) instead of tert-butyl (6S)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **223b**) and phenyl N-(3,4,5-trifluoro-phenyl)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). Example **341** was obtained as a white solid (16.8 mg). LCMS: ($M+H^+$): 407. ^{1}H NMR (400MHz, MeOD) δ ppm 8.72 (d, *J*=0.6 Hz, 2H), 8.18 (s, 1H), 7.32 - 7.23 (m, 2H), 5.50 (d, *J*=18.4 Hz, 1H), 5.00 - 4.93 (m, 1H), 4.80 (d, *J*=18.3 Hz, 1H), 4.37 (dd, *J*=4.3, 12.9 Hz, 1H), 4.25 - 4.19 (m, 1H), 1.27 (d, *J*=6.9 Hz, 3H).

Example 342

(6S)-3-[4-(hydroxymethyl)pyrazol-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: Preparation of methyl 1H-pyrazole-4-carboxylate (compound 342b)

To a solution of 1H-pyrazole-4-carboxylic acid (450.0 mg, 4.01 mmol) in MeOH (15.0 mL) was added $TMSCH_2N_2$ (20.1 mL, 40.1 mmol), and the reaction mixture was stirred at room temperature for 2 hours. The reaction mixture was concentrated to give crude compound **342b** as a white solid (500 mg). LCMS ($M+H^+$): 127. ^1H NMR (400MHz, DMSO-d_6) δ ppm 8.16 - 8.08 (m, 2H), 3.74 (s, 3H).

Step 2: Preparation of methyl tert-butyl (6S)-3-(4-methoxycarbonylpyrazol-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 342c)

To a solution of tert-butyl (6S)-3-iodo-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **102d**,363.0 mg, 1.0 mmol) in CH_3CN (5 mL) was added methyl 1H-pyrazole-4-carboxylate (compound **342b**, 189.2 mg, 1.5 mmol), (1R,2R)-N1,N2-dimethylcyclohexane-1,2-diamine (14.2 mg, 0.1 mmol) , Cs_2CO_3 (651.6 mg, 2.0 mmol) and Cu_2O (18.9 mg, 0.1 mmol) under N_2 at room temperature, and the reaction mixture was stirred at 80 °C for 12 hours. The solvent was removed in *vacuo*, and the residue was purified by silica gel column chromatography(PE/EtOAc: 10/1 to 1/1) to give compound **342c** as a colorless oil (50.0 mg). LCMS: ($M+H^+$): 362.

Step 3: Preparation of methyl 1-[(6S)-6-methyl-5-[(3,4,5-trifluorophenyl)carbamoyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]pyrazole-4-carboxylate (compound 342d)

Compound **342d** was prepared in analogy to the preparation of Example **11** by using 3,4,5-trifluoroaniline instead of 3-(trifluoromethyl)aniline, and methyl tert-butyl (6S)-3-(4-methoxycarbonylpyrazol-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **342c**) instead of tert-butyl 3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-

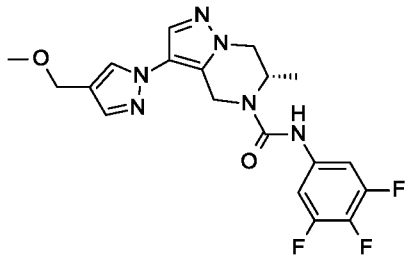
a]pyrazine-5-carboxylate (compound **11a**). Compound **342d** was obtained as white solid (20 mg). LCMS ($M+H^+$): 435.

Step 4: Preparation of (6S)-3-[4-(hydroxymethyl)pyrazol-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 342)

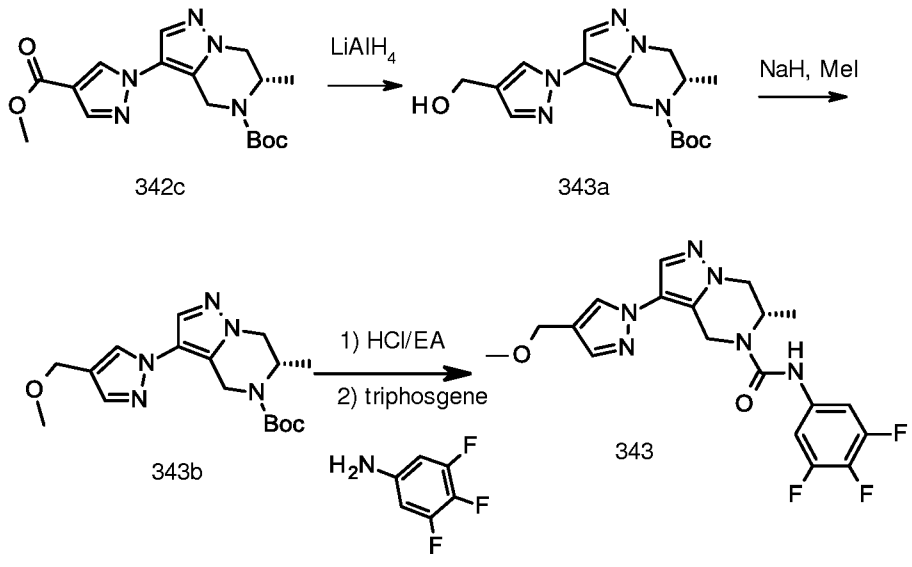
To a solution of methyl 1-[(6S)-6-methyl-5-[(3,4,5-trifluorophenyl)carbamoyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]pyrazole-4-carboxylate (compound **342d**) (20.0 mg, 0.046 mmol) in THF (5.0 mL) was added $LiAlH_4$ (3.5 mg, 0.092 mmol) at 0 °C. The resulting reaction mixture was stirred at 0 °C for 1 hour. After a few drops of water was added, the solvent was removed in *vacuo*, and the residue was purified by prep-HPLC to give Example **342** as white solid (7.7 mg). LCMS: ($M+H^+$): 407. ^1H NMR (400MHz, MeOD) δ ppm 7.94 (s, 1H), 7.82 (s, 1H), 7.69 (s, 1H), 7.31-7.23 (m, 2H),, 5.23 (d, *J*=16.7 Hz, 1H), 4.99 (br. s., 1H), 4.66 (d, *J*=17.2 Hz, 1H), 4.59 (s, 2H), 4.38 - 4.29 (m, 1H), 4.24 - 4.16 (m, 1H), 1.28 (d, *J*=6.7 Hz, 3H).

Example 343

(6S)-3-[4-(methoxymethyl)pyrazol-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: Preparation of tert-butyl (6S)-3-[4-(hydroxymethyl)pyrazol-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 343a)

To a solution of methyl tert-butyl (6S)-3-(4-methoxycarbonylpyrazol-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **342c**, 50.0 mg, 0.14 mmol) in THF (5 mL) was added $LiAlH_4$ (5.3 mg, 0.14 mmol) and the reaction mixture was stirred at 5 °C for 1 hour. The reaction mixture was poured into ice-water (5 mL) and extracted with EtOAc (20 mL), the organic layer was concentrated in *vacuo* to provide the crude product compound **343a** as a yellow oil (30.0 mg). LCMS: ($M+H^+$): 334.2

Step 2: Preparation of tert-butyl (6S)-3-[4-(methoxymethyl)pyrazol-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 343b)

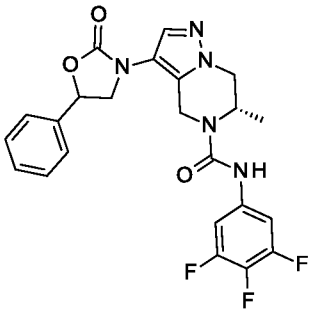
To a solution of tert-butyl (6S)-3-[4-(hydroxymethyl)pyrazol-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **343a**, 30.0 mg, 0.089 mmol) in THF (5 mL) was added NaH (4.32 mg, 0.11 mmol) and CH_3I (15.3 mg, 0.11 mmol) at 0 °C. The reaction mixture was stirred at 30 °C for 1 hour, quenched with aqueous NH_4Cl solution and extracted with EtOAc (20 mL). The organic layer was concentrated to give crude compound **342b** as a colorless oil (30 mg), which was used in next step directly without further purification. LCMS: ($M+H^+$): 348.

Step 3: Preparation of (6S)-3-[4-(methoxymethyl)pyrazol-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 343)

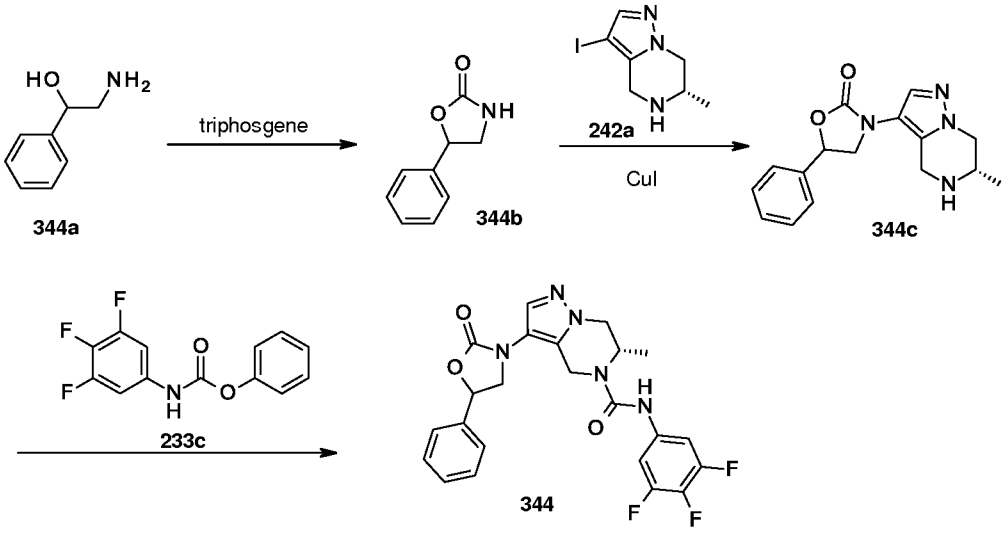
The title compound was prepared in analogy to the preparation of Example **11** by 3,4,5-trifluoroaniline instead of 3-(trifluoromethyl)aniline, and tert-butyl (6S)-3-[4-(methoxymethyl)pyrazol-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **343b**) instead of tert-butyl 3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **11a**). Example **343** was obtained as a white solid (5.3 mg). LCMS: ($M+H^+$): 421. ^1H NMR(400MHz, MeOD) δ ppm 8.01 (s, 1H), 7.85 (s, 1H), 7.72 (s, 1H), 7.34-7.26 (m, 2H),, 5.26 (d, *J*=17.1 Hz, 1H), 5.05 - 4.98 (m, 1H), 4.69 (d, *J*=17.1 Hz, 1H), 4.46 (s, 2H), 4.39 - 4.32 (m, 1H), 4.25 - 4.20 (m, 1H), 3.40 (s, 3H), 1.30 (d, *J*=6.9 Hz, 3H).

Example 344

(6S)-6-methyl-3-(2-oxo-5-phenyl-oxazolidin-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: **preparation of 5-phenyloxazolidin-2-one (compound 344b)**

To a solution of 2-amino-1-phenyl-ethanol (compound **344a**, 1.1 g, 8.0 mmol) and TEA (2.4 g, 24.0 mmol) in DCM (10.0 mL) was added triphosgene (0.71 g, 2.4 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 12 hours, and then concentrated in *vacuo*. The resulting residue was purified by prep-HPLC to give compound **344b** as a white solid (290 mg). LCMS ($M+H^+$): 164.

Step 2: **preparation of 3-[(6S)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl]-5-phenyl-oxazolidin-2-one (compound 344c)**

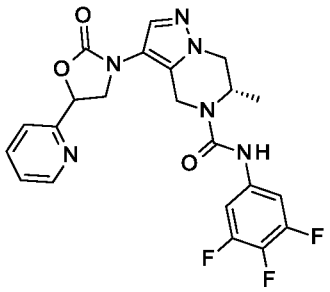
To a solution of 5-phenyloxazolidin-2-one (compound **344b**, 75.1 mg, 0.46 mmol) in dioxane (3 mL) was added (6S)-3-iodo-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **242a**, 100.0 mg, 0.38 mmol), (1R,2R)-N1,N2-dimethylcyclohexane-1,2-diamine (5.6 mg, 0.04 mmol) K_3PO_4 (160.6 mg, 0.76 mmol), and CuI (7.6 mg, 0.04 mmol). The reaction mixture was flushed with nitrogen and stirred at 120 °C for 15 hours. The reaction mixture was then filtered and the filtrate was concentrated in *vacuo*. The resulting residue was purified by silica gel column (DCM: MeOH=30:1-10:1) to give compound **344c** as a yellow oil (80.0 mg). LCMS ($M+H^+$): 299.

Step 3: preparation of (6S)-6-methyl-3-(2-oxo-5-phenyl-oxazolidin-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 344)

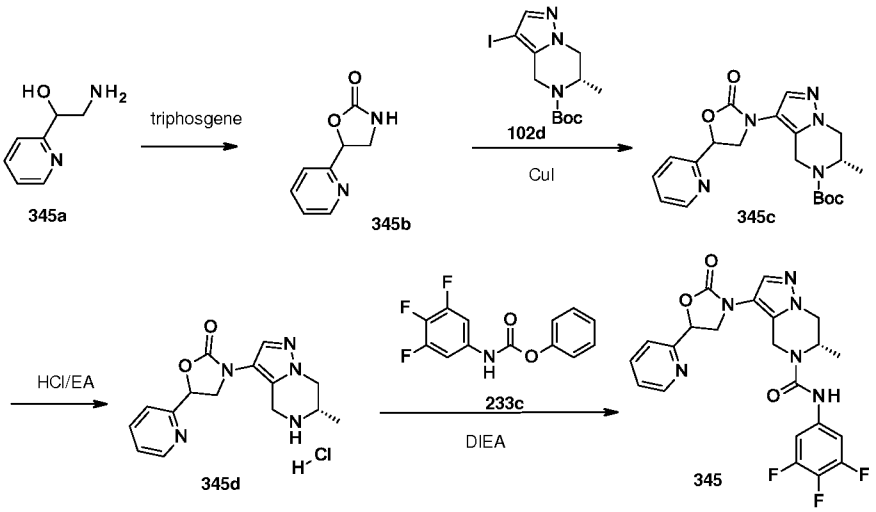
To a solution of 3-[(6S)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl]-5-phenyl-oxazolidin-2-one (compound **344c**, 62.8 mg 0.3 mmol) in DCM (2.0 mL) was added DIPEA (104.5 mg, 0.8 mmol), and a solution of phenyl N-(3,4,5-trifluorophenyl)carbamate (compound **233c**, 80.0 mg 0.27 mmol) in DCM (1.0 mL). The reaction mixture was stirred at 20°C for 3 hrs, and concentrated in *vacuo*. The residue was purified by prep-HPLC to give **Example 344** (16 mg). LCMS ($M+H^+$): 472. ^1H NMR (400MHz, CD_3OD) δ ppm 7.69 (d, *J*=1.76 Hz, 1 H), 7.56 - 7.40 (m, 5 H), 7.29 (ddd, *J*=10.29, 6.40, 3.64 Hz, 2 H), 5.80 (t, *J*=8.16 Hz, 1 H), 5.12 (dd, *J*=16.94, 4.64 Hz, 1 H), 5.02 – 4.94 (m, 1 H), 4.58 (d, *J*=17.32 Hz, 1 H), 4.42 (dt, *J*=13.80, 8.78 Hz, 1 H), 4.35 - 4.27 (m, 1 H), 4.21 - 4.14 (m, 1 H), 3.99 (dt, *J*=11.86, 8.38 Hz, 1 H), 1.32-1.26 (m, 3 H).

Example 345

(6S)-6-methyl-3-[2-oxo-5-(2-pyridyl)oxazolidin-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: **preparation of 5-(2-pyridyl)oxazolidin-2-one (compound 345b)**

To a solution of 2-amino-1-(2-pyridyl)ethanol (compound **345a**, 200.0 mg, 1.45 mmol) in DCM (2 mL) was added DIPEA (560.9 mg, 4.34 mmol) , and triphosgene (214.8 mg, 0.72 mmol). The reaction mixture was stirred at room temperature for 5 hours, and then concentrated in *vacuo* and purified by prep-TLC (DCM:MeOH=10:1) to afford compound **345b** as a yellow oil (107.0 mg). LCMS ($M+H^+$): 165.

Step 2: **preparation of tert-butyl (6S)-6-methyl-3-[2-oxo-5-(2-pyridyl)oxazolidin-3-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 345c)**

To a mixture of 5-(2-pyridyl)oxazolidin-2-one (compound **345b**, 80.0 mg, 0.49 mmol), CuI (18.6 mg, 0.10mmol), K_3PO_4 (206.9 mg, 0.97 mmol) and (1R,2R)-N1,N2-dimethylcyclohexane-1,2-diamine (14.2 mg, 0.10 mmol) in dioxane (2 mL) was added tert-butyl (6S)-3-iodo-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **102d**, 177.0 mg, 0.49 mmol). The reaction mixture was stirred at 100 °C for 15 hours, and then filtered and concentrated in *vacuo*. The resulting residue was purified by prep-TLC (DCM:MeOH=10:1, Rf=0.25) to afford compound **345c** (50.0 mg) as yellow oil. LCMS ($M+H^+$): 400.

Step 3: **preparation of 3-[(6S)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl]-5-(2-pyridyl)oxazolidin-2-one;hydrochloride (compound 345d)**

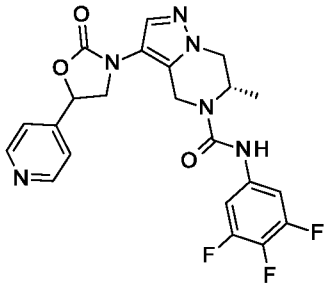
Tert-butyl (6S)-6-methyl-3-[2-oxo-5-(2-pyridyl)oxazolidin-3-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **345c**, 50.0 mg, 0.13 mmol) was dissolved in HCl/EtOAc (2.0 mL) and the reaction mixture was stirred at room temperature for 0.5 hour, and then concentrated to afford compound **345d** as a yellow oil (40.0 mg). LCMS ($M+H^+$): 300.

Step 4: preparation of (6S)-6-methyl-3-[2-oxo-5-(2-pyridyl)oxazolidin-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 345)

To a mixture of 3-[(6S)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl]-5-(2-pyridyl)oxazolidin-2-one (compound **345d**, 40.0 mg, 0.13 mmol), and DIPEA (51.8 mg, 0.40 mmol) in DMF (1 mL) was added phenyl N-(3,4,5-trifluorophenyl)carbamate (compound **233c**, 42.9 mg, 0.16 mmol). The reaction mixture was stirred at room temperature for 5 hours, then was purified by prep-HPLC to afford **Example 345** as a white solid (6.6 mg). LCMS ($M+H^+$): 473. ^1H NMR (400MHz, chloroform-d) δ ppm 8.78 - 8.69 (m, 1H), 8.10 - 8.01 (m, 1H), 7.80 - 7.73 (m, 1H), 7.72 - 7.61 (m, 1H), 7.58 - 7.52 (m, 2H), 7.27 - 7.15 (m, 2H), 6.01 - 5.86 (m, 1H), 5.19 - 5.07 (m, 2H), 4.62 - 4.41 (m, 2H), 4.35 - 4.16 (m, 2H), 4.16 - 4.12 (m, 1H), 1.35-1.29 (m, 3H).

Example 346

(6S)-6-methyl-3-[2-oxo-5-(4-pyridyl)oxazolidin-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

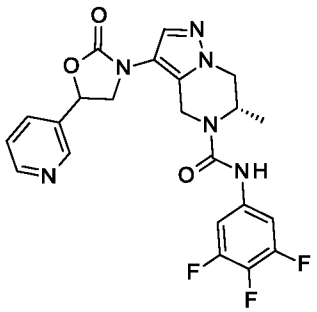


Preparation of (6S)-6-methyl-3-[2-oxo-5-(4-pyridyl)oxazolidin-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 346)

The title compound was prepared in analogy to **Example 345** by using 2-amino-1-(4-pyridyl)ethanol instead of 2-amino-1-(2-pyridyl)ethanol. **Example 346** was obtained as a light yellow solid (60.0 mg). LCMS: ($M+H^+$): 473. ^{1}H NMR (400MHz, MeOD) δ ppm 8.66 (d, *J*=5.8 Hz, 2H), 7.67 (d, *J*=3.8 Hz, 1H), 7.58 (d, *J*=5.5 Hz, 2H), 7.34 - 7.23 (m, 2H), 5.88 (t, *J*=8.0 Hz, 1H), 5.10 (dd, *J*=9.7, 16.9 Hz, 1H), 4.96 (dd, *J*=3.4, 6.7 Hz, 1H), 4.60 - 4.45 (m, 2H), 4.35 - 4.25 (m, 1H), 4.22 - 4.12 (m, 1H), 3.96 (td, *J*=8.2, 12.7 Hz, 1H), 1.32 - 1.21 (m, 3H).

Example 347

(6S)-6-methyl-3-[2-oxo-5-(3-pyridyl)oxazolidin-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



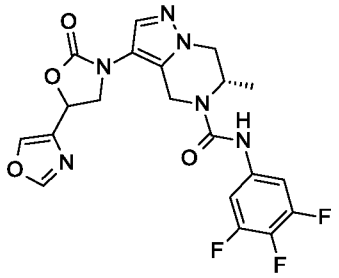
Preparation of (6S)-6-methyl-3-[2-oxo-5-(3-pyridyl)oxazolidin-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 347)

The title compound was prepared in analogy to Example **345** by using 2-amino-1-(3-pyridyl)ethanol instead of 2-amino-1-(2-pyridyl)ethanol. Example **347** was obtained as a light yellow solid (5 mg). LCMS: ($M+H^+$): 473. ^{1}H NMR (400MHz, DMSO-d_6) ppm 9.14 (s, 1H), 8.75 (br. s., 1H), 8.65 (d, *J*=4.0 Hz, 1H), 8.02 (d, *J*=8.3 Hz, 1H), 7.67 (d, *J*=2.8 Hz, 1H), 7.51-7.57 (m, 1H), 7.43 (dd, *J*=10.5, 6.3 Hz, 2H), 5.86 (t, *J*=8.0 Hz, 1H), 5.06 (dd, *J*=16.9, 4.6 Hz,

1H), 4.88 (br. s., 1H), 4.33-4.48 (m, 2H), 4.18-4.26 (m, 1H), 4.10-4.17 (m, 1H), 3.97-4.07 (m, 1H), 1.19-1.12 (m, 3H)

Example 348

(6S)-6-methyl-3-(5-oxazol-4-yl-2-oxo-oxazolidin-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

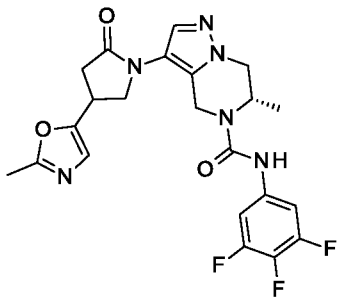


Preparation of (6S)-6-methyl-3-(5-oxazol-4-yl-2-oxo-oxazolidin-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 348)

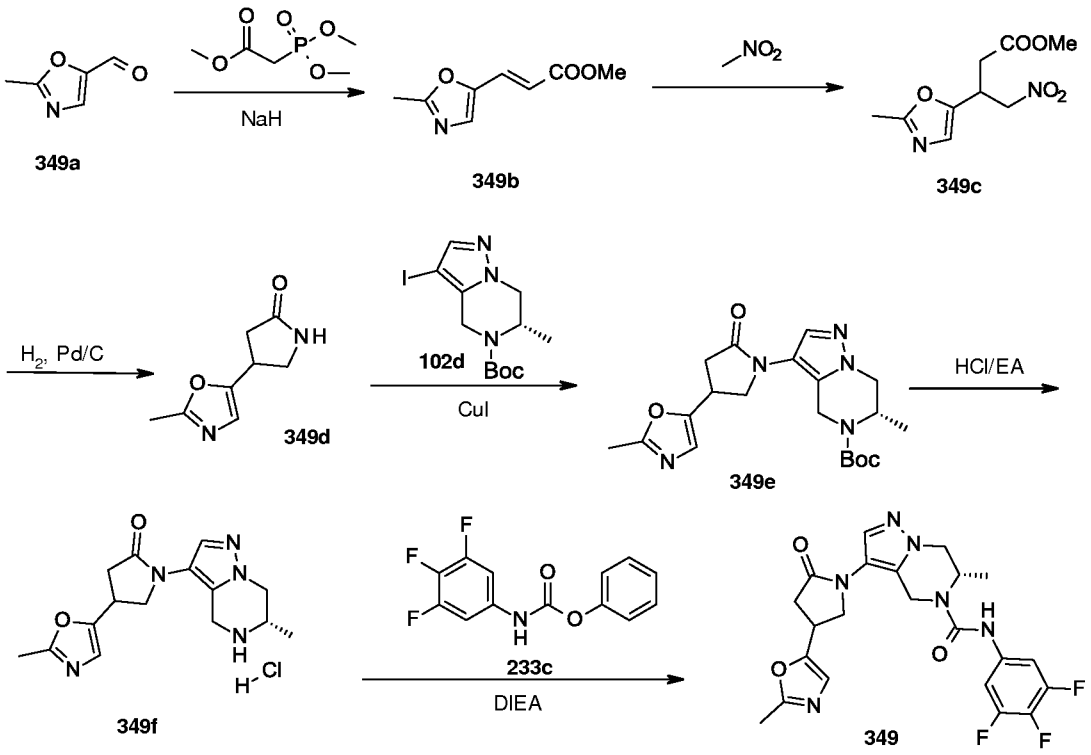
The title compound was prepared in analogy to **Example 289** by using oxazole-4-carbaldehyde instead of 1-methyl-1H-imidazole-2-carbaldehyde. **Example 348** was obtained as a white solid (11 mg). LCMS ($M+H^+$): 463. ^{1}H NMR (400MHz, MeOD) δ ppm 8.34 (s, 1H), 8.20 (s, 1H), 7.70 (s, 1H), 7.36 - 7.25 (m, 2H), 5.85 (t, *J*=7.8 Hz, 1H), 5.15 (dd, *J*=10.9, 16.9 Hz, 1H), 5.04 - 4.96 (m, 1H), 4.59 (dd, *J*=4.6, 16.9 Hz, 1H), 4.40 - 4.29 (m, 2H), 4.23 - 4.14 (m, 2H), 1.31-1.25 (m, 3H).

Example 349

(6S)-6-methyl-3-[4-(2-methyloxazol-5-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of methyl (E)-3-(2-methyloxazol-5-yl)prop-2-enoate (compound 349b)

To a solution of 2-methyloxazole-5-carbaldehyde (compound **349a**, 1.4 g, 12.6 mmol) and methyl 2-dimethoxyphosphorylacetate (4.7 g, 13.7 mmol) in THF (30.0 mL) was added NaH (1.0 g, 25.2 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for 12 hours, and then quenched with ice-water (20 mL) and extracted with ethyl acetate. The organic layer was washed with brine and dried over Na_2SO_4, and evaporated to give crude compound **349b** (2.0 g) which was used in the next step without further purification. LCMS ($M+H^+$): 168.

Preparation of methyl 3-(2-methyloxazol-5-yl)-4-nitro-butanoate (compound 349c)

To a solution of (E)-3-(2-methyloxazol-5-yl)prop-2-enoate (compound **349b**, 2.0 g, 12.0 mmol) in nitromethane (20 mL) was added DBU (2.0 g, 13.2 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for 12 hours, then concentrated and purified by silica gel column to give compound **349c** as a yellow oil (1.9 g). LCMS ($M+H^+$): 229.

Preparation of 4-(2-methyloxazol-5-yl)pyrrolidin-2-one (compound 349d)

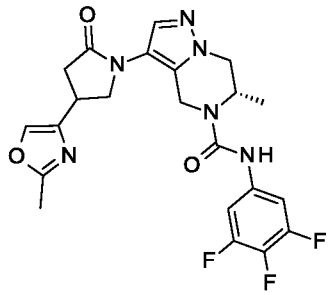
A reaction mixture of methyl 3-(2-methyloxazol-5-yl)-4-nitro-butanoate (compound **349c**, 1.9 g, 8.3 mmol) and Pd/C (200 mg) in methanol (20 mL) was stirred at 50 °C for 12 hours under H_2 at 1 atm, then concentrated and purified by prep-HPLC to give compound **349d** as a white solid (260 mg). LCMS ($M+H^+$): 167.

Preparation of (6S)-6-methyl-3-[4-(2-methyloxazol-5-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 349)

The title compound was prepared in analogy to **Example 345** by using 4-(2-methyloxazol-5-yl)pyrrolidin-2-one (compound **349d**) instead of 5-(2-pyridyl)oxazolidin-2-one (compound **345b**). **Example 349** was obtained as a white solid (20 mg). LCMS ($M+H^+$): 475. ^1H NMR (400MHz, MeOD) δ ppm 7.66 (s, 1 H), 7.28 (dd, *J*=10.29, 6.53 Hz, 2 H), 6.95 (s, 1 H), 5.09 - 5.00 (m, 1 H), 4.99 - 4.93 (m, 1 H), 4.50 (dd, *J*=16.94, 1.63 Hz, 1 H), 4.30 (dd, *J*=12.67, 3.64 Hz, 1 H), 4.23 - 4.12 (m, 2 H), 4.03 – 3.89 (m, 2 H), 2.97 (dd, *J*=17.07, 8.78 Hz, 1 H), 2.77 (dd, *J*=17.19, 7.40 Hz, 1 H), 2.46 (d, *J*=1.25 Hz, 3 H), 1.31-1.29 (m, 3 H).

Example 350

(6S)-6-methyl-3-[4-(2-methyloxazol-4-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

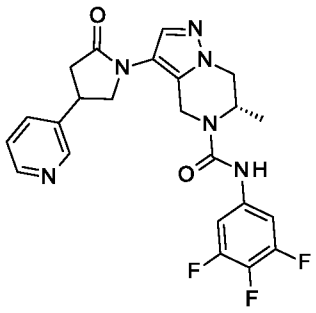


Preparation of (6S)-6-methyl-3-[4-(2-methyloxazol-4-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 350)

The title compound was prepared in analogy to **Example 349** by using 2-methyloxazole-4-carbaldehyde instead of 2-methyloxazole-5-carbaldehyde. **Example 350** was obtained as a white solid (25 mg). LCMS ($M+H^+$): 475. ^1H NMR (400MHz, MeOD) δ ppm 7.75 (d, *J*=1.25 Hz, 1 H), 7.65 (s, 1 H), 7.29 (dd, *J*=10.92, 6.40 Hz, 2 H), 5.06 (dd, *J*=17.07, 5.27 Hz, 1 H), 5.00 – 4.93 (m, 1 H), 4.52 (dd, *J*=16.94, 5.90 Hz, 1 H), 4.30 (dd, *J*=12.80, 4.52 Hz, 1 H), 4.20 - 4.08 (m, 2 H), 3.93 - 3.75 (m, 2 H), 2.96 - 2.87 (m, 1 H), 2.73 (dd, *J*=17.07, 7.53 Hz, 1 H), 2.47 (s, 1.5 H), 2.46 (s, 1.5 H), 1.31-1.29 (m, 3 H).

Example 351

(6S)-6-methyl-3-[2-oxo-4-(3-pyridyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

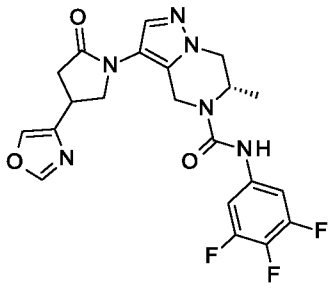


Preparation of (6S)-6-methyl-3-[2-oxo-4-(3-pyridyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 351)

The title compound was prepared in analogy to **Example 349** by using pyridine-3-carbaldehyde instead of 2-methyloxazole-5-carbaldehyde. **Example 351** was obtained as a white solid (15 mg). LCMS ($M+H^+$): 471. ^{1}H NMR (400MHz, MeOD) δ ppm 8.70 - 8.42 (m, 2H), 7.94 (d, *J*=7.9 Hz, 1H), 7.66 (d, *J*=1.0 Hz, 1H), 7.54 - 7.44 (m, 1H), 7.27 (dd, *J*=6.4, 10.3 Hz, 2H), 5.08 (dd, *J*=11.2, 16.9 Hz, 1H), 4.98 - 4.93 (m, 1H), 4.53 (dd, *J*=13.1, 16.9 Hz, 1H), 4.30 - 4.13 (m, 3H), 3.98 - 3.90 (m, 2H), 3.04 - 2.96 (m, 1H), 2.82 - 2.74 (m, 1H), 1.29-1.23 (m, 3H).

Example 352

(6S)-6-methyl-3-(4-oxazol-4-yl-2-oxo-pyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



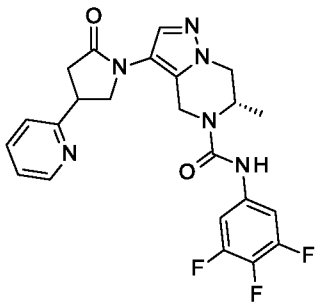
Preparation of (6S)-6-methyl-3-(4-oxazol-4-yl-2-oxo-pyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 352)

The title compound was prepared in analogy to **Example 349** by using oxazole-4-carbaldehyde instead of 2-methyloxazole-5-carbaldehyde. **Example 352** was obtained as a white solid (11 mg). LCMS ($M+H^+$): 461. ^{1}H NMR (400MHz, MeOD) δ ppm 8.23 (s, 1 H), 7.92 (s, 1 H), 7.65 (d, *J*=1.25 Hz, 1 H), 7.34 - 7.24 (m, 2 H), 5.07 (dd, *J*=16.94, 4.89 Hz, 1 H), 5.00 –

4.95 (m, 1 H), 4.52 (dd, *J*=17.07, 4.27 Hz, 1 H), 4.30 (dd, *J*=12.67, 4.39 Hz, 1 H), 4.22 - 4.11 (m, 2 H), 3.98 - 3.82 (m, 2 H), 2.94 (dd, *J*=17.07, 8.78 Hz, 1 H), 2.83 - 2.70 (m, 1 H), 1.28 (d, *J*=7.03 Hz, 3 H).

Example 353

(6S)-6-methyl-3-[2-oxo-4-(2-pyridyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

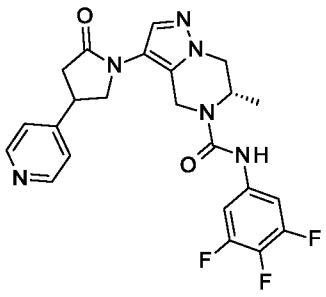


Preparation of (6S)-6-methyl-3-[2-oxo-4-(2-pyridyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 353)

The title compound was prepared in analogy to **Example 349** by using pyridine-2-carbaldehyde instead of 2-methyloxazole-5-carbaldehyde. **Example 353** was obtained as a white solid (56 mg). LCMS ($M+H^+$): 471. ^{1}H NMR (400MHz, MeOD) δ ppm 8.57 (d, *J*=4.8 Hz, 1H), 7.80 (tt, *J*=1.9, 7.7 Hz, 1H), 7.64 (d, *J*=1.3 Hz, 1H), 7.46 - 7.40 (m, 1H), 7.34 - 7.23 (m, 3H), 5.07 (dd, *J*=11.1, 16.9 Hz, 1H), 4.99 - 4.91 (m, 1H), 4.53 (dd, *J*=9.0, 16.9 Hz, 1H), 4.31 - 4.12 (m, 3H), 4.06 - 3.97 (m, 2H), 3.01 - 2.85 (m, 2H), 1.29-1.23 (m, 3H).

Example 354

(6S)-6-methyl-3-[2-oxo-4-(4-pyridyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

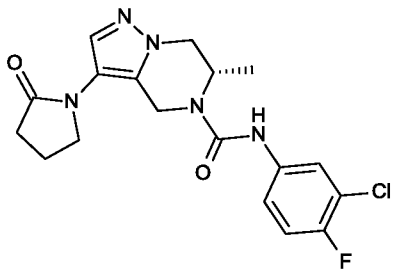


Preparation of (6S)-6-methyl-3-[2-oxo-4-(4-pyridyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 354)

The title compound was prepared in analogy to **Example 349** by using pyridine-4-carbaldehyde instead of 2-methyloxazole-5-carbaldehyde. **Example 354** was obtained as a white solid (17 mg). LCMS (M+H+): 471. ^{1}H NMR (400MHz, MeOD) δ ppm 9.20 (d, *J*=6.0 Hz, 1H), 8.57 (br. s., 2H), 7.63 (d, *J*=3.6 Hz, 1H), 7.52 - 7.33 (m, 4H), 5.12 - 4.94 (m, 1H), 4.92 - 4.76 (m, 1H), 4.52 - 4.32 (m, 1H), 4.25 - 4.05 (m, 3H), 3.88 - 3.75 (m, 2H), 2.85 (dd, *J*=8.5, 16.9 Hz, 1H), 2.69 - 2.61 (m, 1H), 1.18-1.12 (m, 3H).

Example 355:

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

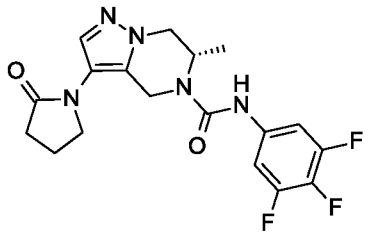


Preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 355):

The title compound was prepared in analogy to Example **223** by using phenyl N-(3-chloro-4-fluoro-phenyl)carbamate (compound **12i**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl] (compound **218c**). **Example 355** was obtained as a solid (100 mg). LCMS (M+H$^+$): 392. ^{1}H NMR (400MHz, chloroform-d) δ ppm 7.65 (dd, *J*=2.6, 6.7 Hz, 2H), 7.43 (s, 1H), 7.35 - 7.29 (m, 1H), 7.10 - 7.02 (m, 1H), 5.18 - 5.05 (m, 2H), 4.43 - 4.35 (m, 1H), 4.34 - 4.26 (m, 1H), 4.07 - 4.01 (m, 1H), 3.99 - 3.90 (m, 1H), 3.82 - 3.73 (m, 1H), 2.66 - 2.57 (m, 2H), 2.34 - 2.21 (m, 2H), 1.38 (d, *J*=7.0 Hz, 3H).

Example 356:

(6S)-6-methyl-3-(2-oxopyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

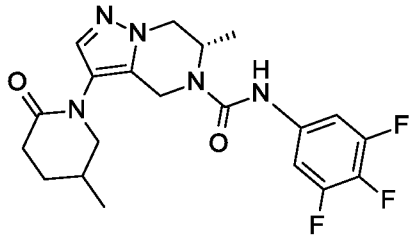


Preparation of (6S)-6-methyl-3-(2-oxopyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 356):

The title compound was prepared in analogy to **Example 223** by using phenyl N-(3,4,5-trifluorophenyl)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl] (compound **218c**). **Example 356** was obtained as a solid (933 mg). LCMS ($M+H^+$): 394. ^1H NMR (400MHz, CD_3OD) δ ppm 7.63 (s, 1H), 7.34 - 7.24 (m, 2H), 5.08 - 5.00 (m, 1H), 5.00 - 4.93 (m, 1H), 4.55 - 4.47 (m, 1H), 4.34 - 4.25 (m, 1H), 4.21 - 4.11 (m, 1H), 3.94 - 3.81 (m, 2H), 2.62 - 2.52 (m, 2H), 2.31 - 2.19 (m, 2H), 1.27 (d, *J*=7.0 Hz, 3H).

Example 358:

(6S)-6-methyl-3-(5-methyl-2-oxo-1-piperidyl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

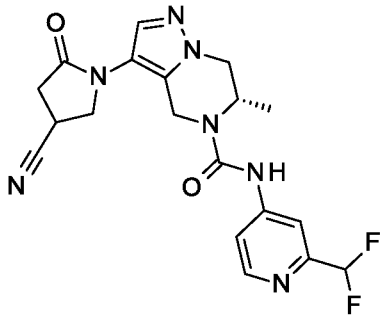


Preparation of (6S)-6-methyl-3-(5-methyl-2-oxo-1-piperidyl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 358):

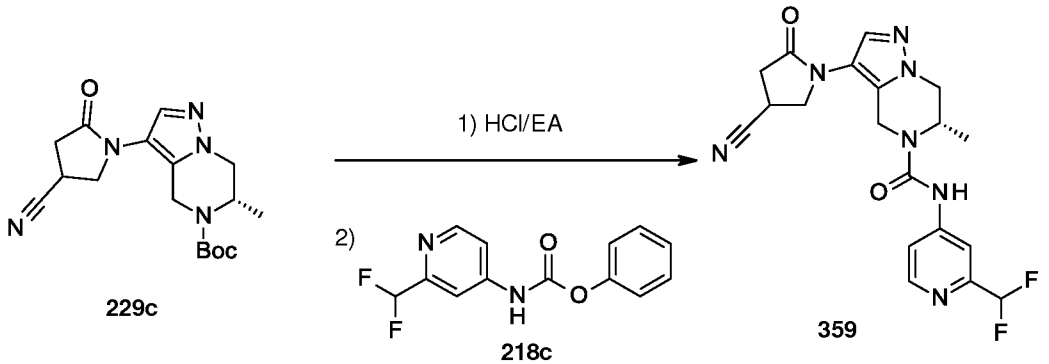
The title compound was prepared in analogy to **Example 223** by using 5-methylpiperidin-2-one instead of pyrrolidin-2-one, and phenyl N-(3,4,5-trifluorophenyl)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl] (compound **218c**). **Example 358** was obtained as a solid (24 mg). LCMS ($M+H^+$): 422. ^1H NMR (400MHz, chloroform-d) δ ppm 8.22 (s, 0.5H), 7.98 (s, 0.5H), 7.48 (s, 0.5H), 7.47 (s, 0.5H), 7.36 - 7.29 (m, 1H), 7.28 - 7.22 (m, 1H), 5.07 (m, 1H), 4.89 (d, *J*=17.1 Hz, 0.5H), 4.78 (d, *J*=16.8 Hz, 0.5H), 4.32-4.15 (m, 2H), 4.06 - 3.96 (m, 1H), 3.83 - 3.74 (m, 0.5H), 3.62 - 3.48 (m, 1H), 3.31 (dd, *J*=10.0, 12.0 Hz, 0.5H), 2.75 - 2.54 (m, 2H), 2.28 - 2.09 (m, 1H), 2.06 - 1.96 (m, 1H), 1.65 - 1.56 (m, 1H), 1.45 - 1.36 (m, 3H), 1.16-1.10 (m, 3H).

Example 359:

(6S)-3-(4-cyano-2-oxo-pyrrolidin-1-yl)-N-[2-(difluoromethyl)-4-pyridyl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:

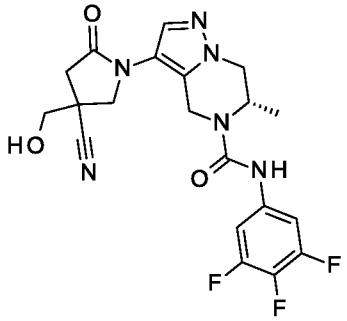


Preparation of (6S)-3-(4-cyano-2-oxo-pyrrolidin-1-yl)-N-[2-(difluoromethyl)-4-pyridyl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 240):

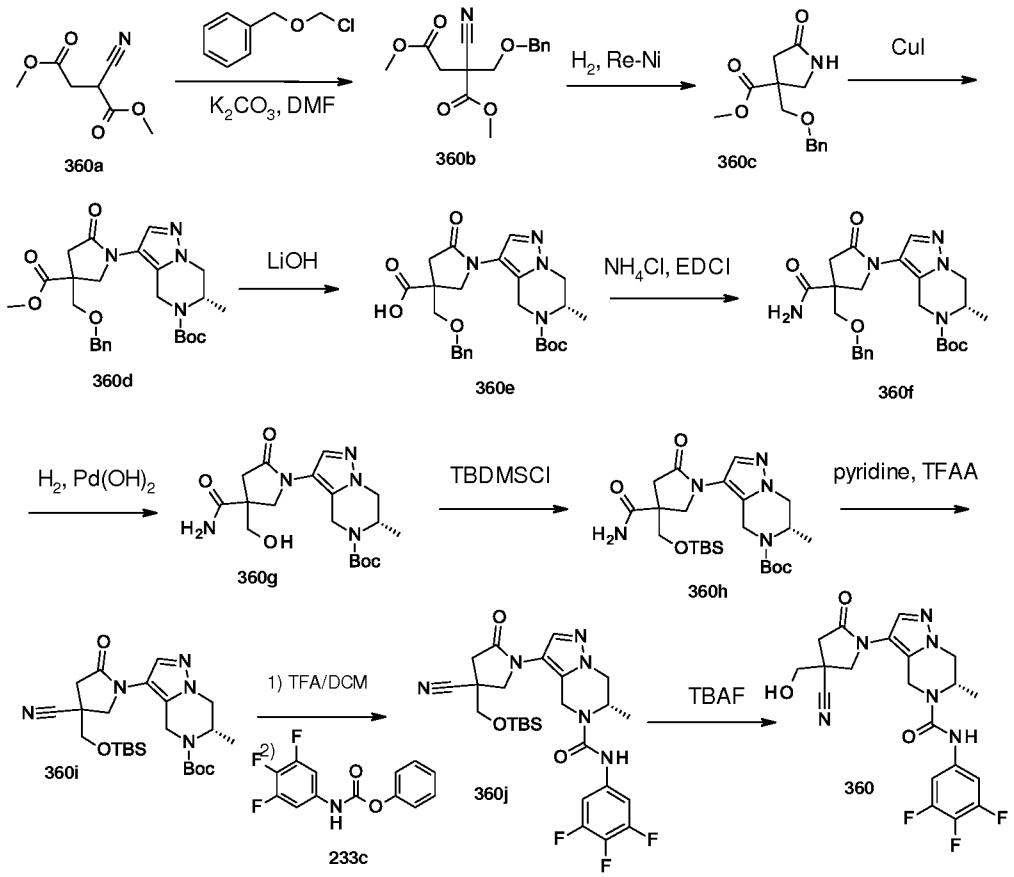
The title compound was prepared in analogy to **Example 229** by using phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**) instead of phenyl N-(3-chloro-4-fluoro-phenyl)carbamate (compound **12i**). **Example 359** was obtained as a solid (14 mg). LCMS ($M+H^+$): 416. ^1H NMR (400MHz, chloroform-d) δ ppm 8.49 (d, *J*=4.8 Hz, 1H), 7.99 (s, 0.5H), 7.91 (s, 0.5H), 7.80-7.75 (m, 1H), 7.66 - 7.60 (m, 1H), 7.46 (s, 0.5H), 7.43 (s, 0.5H), 6.76 - 6.44 (m, 1H), 5.17 - 5.03 (m, 2H), 4.46-4.39 (m, 1H), 4.39-4.31 (m, 1H), 4.29 - 4.02 (m, 3H), 3.68 - 3.53 (m, 1H), 3.12 - 2.94 (m, 2H), 1.43 (d, *J*=6.8 Hz, 1.5H), 1.40 (d, *J*=7.0 Hz, 1.5H).

Example 360:

(6S)-3-[4-cyano-4-(hydroxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: **preparation of dimethyl 2-((benzyloxy)methyl)-2-cyanosuccinate (compound 360b)**

To a solution of dimethyl 2-cyanosuccinate (compound **360a**, 342 mg, 2 mmol) in DMF (3 mL) was added ((chloromethoxy)methyl)benzene (470 mg, 417 μL, 3 mmol) and K_2CO_3 (553 mg, 4 mmol). The reaction mixture was stirred at 40°C for 2 hours. The reaction mixture was diluted with PE/EtOAc (v/v=2/1), and washed with water. The aqueous phase was extracted with PE/EtOAc (v/v=2/1) twice. The combined organic phase was concentrated, and the residue was purified by silica gel column to give compound **360b** (470 mg). LCMS ($M+H^+$): 292.

Step 2: preparation of methyl 3-((benzyloxy)methyl)-5-oxopyrrolidine-3-carboxylate (compound 360c)

To a suspension of Raney nickel (138 mg, 1.61 mmol) (pre-washed by methanol) in MeOH (10 mL) was added dimethyl 2-((benzyloxy)methyl)-2-cyanosuccinate (compound **360b**, 470 mg, 1.61 mmol) in MeOH (1 mL). The reaction mixture was flushed with hydrogen and stirred at 40 °C overnight. The reaction mixture was filtered and concentrated to give crude compound **360c** (370 mg). LCMS ($M+H^+$): 264.

Step 3: preparation of (6S)-tert-butyl 3-(4-((benzyloxy)methyl)-4-(methoxycarbonyl)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 360d)

The reaction mixture of methyl 3-((benzyloxy)methyl)-5-oxopyrrolidine-3-carboxylate (compound **360c**, 370 mg, 1.41 mmol), (6S)-3-iodo-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **102d**, 459 mg, 1.26 mmol), K_3PO_4 (597 mg, 2.81 mmol), CuI (53.5 mg, 281 μmol) and (1R,2R)-N1,N2-dimethylcyclohexane-1,2-diamine (40 mg, 281 μmol) in DMSO (15 mL) was flushed with nitrogen and sealed. The reaction mixture was stirred at 105 °C in microwave for 2 hours. After cooled down, the reaction mixture was diluted with EtOAc, and washed with water. The aqueous phase was extracted with EtOAc three times. The combined organic layer was dried over Na_2SO_4, and concentrated in *vacuo*. The residue was purified by silica gel column to give compound **360d** (561 mg). LCMS ($M+H^+$): 499.

Step 4: preparation of 3-((benzyloxy)methyl)-1-((S)-5-(tert-butoxycarbonyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)-5-oxopyrrolidine-3-carboxylic acid (compound 360e)

To a solution of compound (6S)-tert-butyl 3-(4-((benzyloxy)methyl)-4-(methoxycarbonyl)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **360d**, 561 mg, 1.13 mmol) in THF (2.5 mL) was added a solution of lithium hydroxide monohydrate (236 mg, 5.63 mmol) in water (2.5 mL). The reaction mixture was stirred at room temperature for 1 hour, then acidified with 1N HCl aqueous solution to pH 5.0, and extracted with DCM twice. The combined organic phase was dried over Na_2SO_4, filtrated and concentrated to give crude product **360e** (518 mg) which was used directly for next step without further purification. LCMS ($M+H^+$): 485.

Step 5: preparation of (6S)-tert-butyl 3-(4-((benzyloxy)methyl)-4-carbamoyl-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 360f)

To a solution of compound 3-((benzyloxy)methyl)-1-((S)-5-(tert-butoxycarbonyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)-5-oxopyrrolidine-3-carboxylic acid (compound **360e**, 570 mg, 1.18 mmol) in DCM (10 mL) was added ammonia hydrochloride (189 mg, 3.53 mmol), EDCI (293 mg, 1.53 mmol), DIPEA (1.55 g, 2.05 mL, 12 mmol) and hydroxybenzotriazole (47.7 mg, 353 μmol). The reaction mixture was sealed and stirred at 50 °C for 4 hours. The reaction mixture was washed with water, and the aqueous phase was extracted with DCM twice. The combined organic phase was dried over Na_2SO_4, filtered and concentrated to give crude compound **360f** (569 mg) which was used directly for next step without further purification. LCMS ($M+H^+$): 484.

Step 6: preparation of tert-butyl (6S)-3-[4-carbamoyl-4-(hydroxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 360g)

To a solution of compound (6S)-tert-butyl 3-(4-((benzyloxy)methyl)-4-carbamoyl-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **360f**, 569 mg, 1.18 mmol) in EtOH (5 mL) was added palladium hydroxide on carbon (165 mg, 1.18 mmol). The reaction mixture was stirred at 50 °C for 3 hours under H_2 at 1 atm. The reaction mixture was filtrated and concentrated to give crude product **360g** (463 mg) which was used directly for next step without further purification. LCMS ($M+H^+$): 394.

Step 7: preparation of (6S)-tert-butyl 3-(4-(((tert-butyldimethylsilyl)oxy)methyl)-4-carbamoyl-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 360h)

To a solution of compound (6S)-tert-butyl 3-(4-carbamoyl-4-(hydroxymethyl)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **360g**, 463 mg, 1.18 mmol) in DMF (3 mL) were added imidazole (160 mg, 2.35 mmol), and tert-butyldimethylchlorosilane (355 mg, 2.35 mmol). After stirred at 35°C for 3 hours, the reaction mixture was quenched with ice-water, extracted with EtOAc twice. The combined organic phase was dried over Na_2SO_4 and concentrated to give crude compound **360h** (597 mg) which was used directly for next step without further purification. LCMS ($M+H^+$): 508.

Step 8: preparation of (6S)-tert-butyl 3-(4-(((tert-butyldimethylsilyl)oxy)methyl)-4-cyano-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 360i)

To a solution of compound (6S)-tert-butyl 3-(4-(((tert-butyldimethylsilyl)oxy)methyl)-4-carbamoyl-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **360h**, 597 mg, 1.18 mmol) in dry THF (5 mL) was added pyridine (489 mg, 0.5 mL, 6.18 mmol). The reaction mixture was flushed with N_2 and cooled to 0°C, to which was added dropwise a solution of trifluoroacetic anhydride (752 mg, 0.5 mL, 3.58 mmol) in dry THF (0.5 mL). The resulting reaction mixture was stirred at 0 °C for 3 hours, quenched with ice-water, and extracted with EtOAc twice. The organic phase was dried over Na_2SO_4, and concentrated. The residue was purified by silica gel column to give compound **360i** (350 mg). LCMS ($M+H^+$): 490.

Step 9: preparation of (6S)-3-(4-(((tert-butyldimethylsilyl)oxy)methyl)-4-cyano-2-oxopyrrolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxamide (compound 360j)

The reaction mixture of compound (6S)-tert-butyl 3-(4-(((tert-butyldimethylsilyl)oxy)methyl)-4-cyano-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **360i**, 350 mg, 715 μmol) and trifluoroacetic acid (2.96 g, 2 mL, 26 mmol) in DCM (1 mL) was stirred at room temperature for 30 minutes. The reaction mixture was concentrated, then toluene was added for azeotropic distillation. The residue was dissolved in DMF (2 mL), to which were added DIPEA (754 mg, 1 mL, 5.83 mmol) and phenyl (3,4,5-trifluorophenyl)carbamate (compound **233c**,191 mg, 715 μmol). The reaction mixture was stirred for 3 hours at 40°C, then quenched with ice-water, and extracted with EtOAc twice. The combined organic phase was dried over Na_2SO_4 and concentrated. The residue was purified by silica gel column to give compound **360j** (330 mg). LCMS ($M+H^+$): 563.

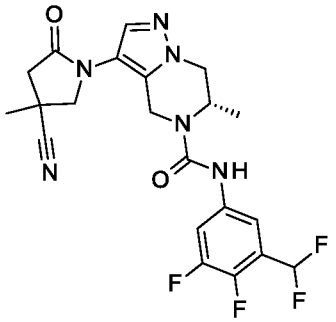
Step 10: preparation of (6S)-3-[4-cyano-4-(hydroxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 360)

To a solution of compound (6S)-3-(4-(((tert-butyldimethylsilyl)oxy)methyl)-4-cyano-2-oxopyrrolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxamide (compound **360j**, 330 mg, 587 μmol) in THF (2 mL) was added tetrabutylammonium fluoride (1.81 g, 2 mL, 2 mmol). The reaction mixture was stirred at room

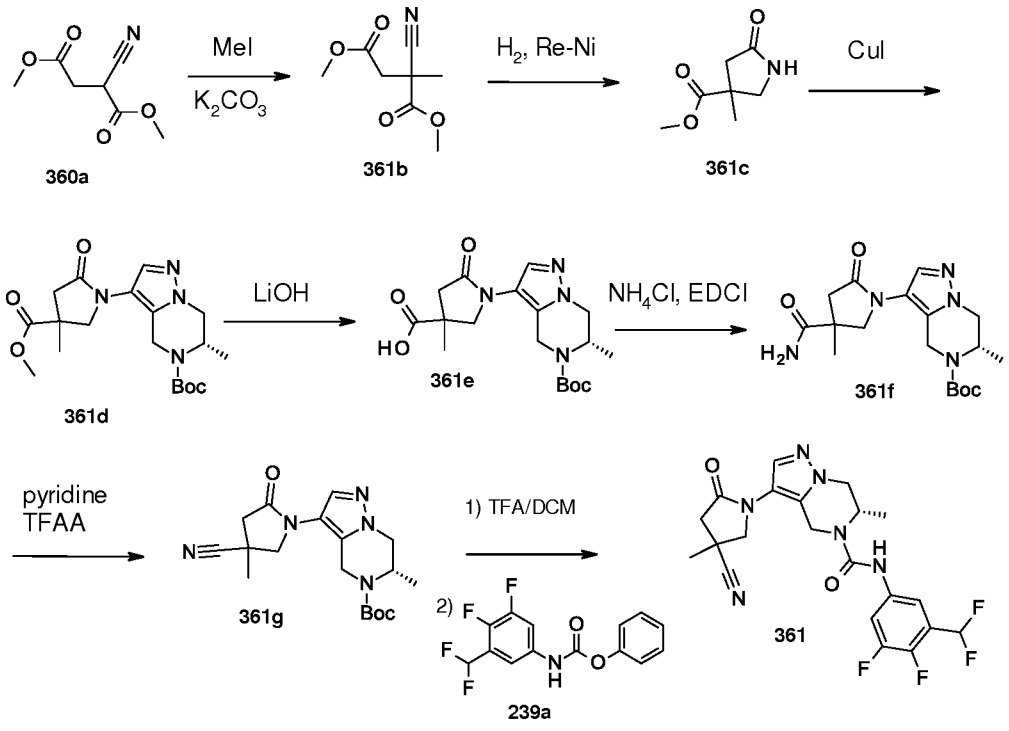
temperature for 2 hours, and then washed with brine. The aqueous phase was extracted with EtOAc twice. The combined organic phase was dried over Na_2SO_4 and concentrated. The residue was purified by silica gel column to give **Example 360** (150 mg). LCMS ($M+H^+$): 449. ^1H NMR (400MHz, CD_3OD) δ ppm 7.66 (s, 0.5H), 7.65 (s, 0.5H), 7.35 - 7.19 (m, 2H), 5.06 (d, *J*=5.0 Hz, 0.5H), 5.01 (d, *J*=4.8 Hz, 0.5H), 4.99 - 4.92 (m, 1H), 4.50 (d, *J*=17.1 Hz, 1H), 4.36-4.26 (m, 1H), 4.24 - 4.08 (m, 3H), 4.04-3.96 (m, 1H), 3.88-3.80 (m, 2H), 3.07 - 2.99 (m, 1H), 2.91 - 2.81 (m, 1H), 1.30 - 1.26 (m, 3H).

Example 361:

(6S)-3-(4-cyano-4-methyl-2-oxo-pyrrolidin-1-yl)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of methyl 3-methyl-5-oxo-pyrrolidine-3-carboxylate (compound 361c)

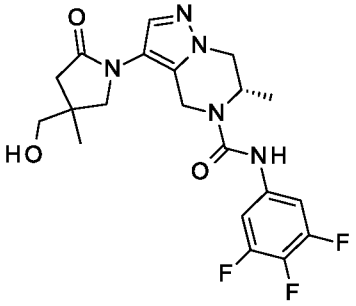
Methyl 3-methyl-5-oxo-pyrrolidine-3-carboxylate (compound **361c**) was prepared in analogy to methyl 3-((benzyloxy)methyl)-5-oxopyrrolidine-3-carboxylate (compound **360c**) by using methyl iodide instead of ((chloromethoxy)methyl)benzene.

Preparation of (6S)-3-(4-cyano-4-methyl-2-oxo-pyrrolidin-1-yl)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 361):

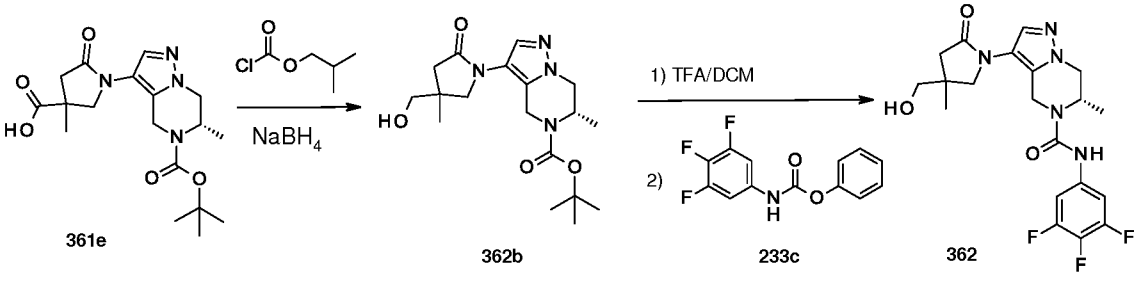
The title compound was prepared in analogy to Example **229** by using methyl 3-methyl-5-oxo-pyrrolidine-3-carboxylate (compound **361c**) instead of methyl 5-oxopyrrolidine-3-carboxylate, and phenyl N-[3-(difluoromethyl)-4,5-difluoro-phenyl]carbamate (compound **239a**) instead of phenyl N-(3-chloro-4-fluoro-phenyl)carbamate . **Example 361** was obtained as a solid (64 mg). LCMS ($M+H^+$):465. ^1H NMR (400MHz, CD_3OD) δ ppm 7.75 - 7.62 (m, 2H), 7.45 (br. s., 1H), 7.19 - 6.84 (m, 1H), 5.08 (d, *J*=6.8 Hz, 0.5H), 5.04 (d, *J*=7.0 Hz, 0.5H),, 5.01 - 4.93 (m, 1H), 4.57-4.47 (m, 1H), 4.36 - 4.15 (m, 3H), 3.92-3.85 (m, 1H), 3.09 (d, *J*=17.1 Hz, 1H), 2.75 (d, *J*=17.1 Hz, 1H), 1.69 (s, 3H), 1.28 (d, *J*=7.0 Hz, 3H).

Example 362:

(6S)-3-[4-(hydroxymethyl)-4-methyl-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: **preparation of (6S)-tert-butyl 3-(4-(hydroxymethyl)-4-methyl-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 362b)**

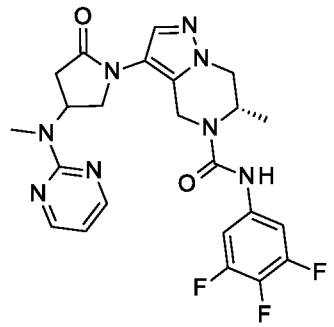
To a mixture of compound 1-((S)-5-(tert-butoxycarbonyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)-3-methyl-5-oxopyrrolidine-3-carboxylic acid (compound **361e**, 189 mg, 0.5 mmol) and 4-methylmorpholine (75.9 mg, 82.5 μL, 750 μmol) in dry THF (3 mL) at -10°C was added dropwise isobutyl chloroformate (81.9 mg, 78.2 μL, 600 μmol). After stirred at the same temperature for 2 hours, the reaction mixture was added dropwise to a mixture of sodium borohydride (37.8 mg, 1 mmol) and ice (3 g). The reaction mixture was extracted with DCM twice, the organic phase was combined and concentrated. The residue was purified by silica gel column to give compound **362b** (100 mg). LCMS ($M+H^+$): 365.

Step 2: preparation of (6S)-3-[4-(hydroxymethyl)-4-methyl-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 362)

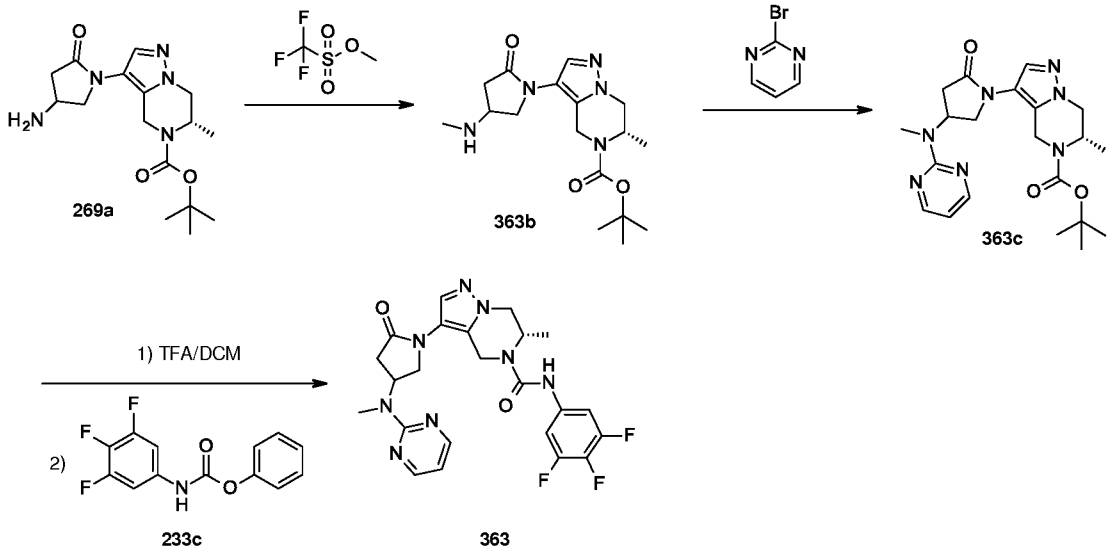
A solution of compound (6S)-tert-butyl 3-(4-(hydroxymethyl)-4-methyl-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **362b**, 100 mg, 274 μmol) in trifluoroacetic acid (2 mL) and DCM (1 mL) was stirred at room temperature for 1 hour. The reaction mixture was concentrated. The residue was dissolved in DMF (2 mL) , to which was added DIPEA (371 mg, 0.5 mL, 2.87 mmol), and phenyl (3,4,5-trifluorophenyl)carbamate (compound **233c**, 95.3 mg, 357 μmol). The reaction mixture was stirred at 50 °C for 2 hours, then was purified by prep-HPLC to give **Example 362** (46 mg). LCMS ($M+H^+$): 438. ^{1}H NMR (400MHz, CD_3OD) δ ppm 7.63 (s, 1H), 7.34-7.23 (m, 2H), 5.05 (d, *J*=4.5 Hz, 0.5H), 5.01 (d, *J*=4.6 Hz, 0.5H), 4.99 - 4.92 (m, 1H), 4.54 - 4.46 (m, 1H), 4.35 - 4.27 (m, 1H), 4.19 - 4.12 (m, 1H), 3.83 - 3.75 (m, 1H), 3.58 - 3.48 (m, 3H), 2.63-2.55 (m, 1H), 2.36-2.29 (m, 1H), 1.30 - 1.23 (m, 6H).

Example 363:

(6S)-6-methyl-3-[4-[methyl(pyrimidin-2-yl)amino]-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: **preparation of (6S)-tert-butyl 6-methyl-3-(4-(methylamino)-2-oxopyrrolidin-1-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 363b)**

To a solution of compound (6S)-tert-butyl 3-(4-amino-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **269a**, 33.5 mg, 0.1 mmol) in 1,1,1,3,3,3-hexafluoro-2-propanol (810 mg, 0.5 mL) was added methyl trifluoromethanesulfonate (24.6 mg, 17 μL, 150 μmol) in 1,1,1,3,3,3-hexafluoro-2-propanol (324 mg, 0.2 mL). The resulting mixture was stirred at room temperature for 5 hours, and then concentrated. The residue was purified by silica gel column to give compound **363b** (17.5 mg). LCMS ($M+H^+$): 350.

Step 2: preparation of (6S)-tert-butyl 6-methyl-3-(4-(methyl(pyrimidin-2-yl)amino)-2-oxopyrrolidin-1-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 363c)

To a solution of compound (6S)-tert-butyl 6-methyl-3-(4-(methylamino)-2-oxopyrrolidin-1-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (**compound 363b**, 34.9 mg, 0.1 mmol) in DMF (1 mL) was added DIPEA (377 mg, 0.5 mL, 2.92 mmol), potassium iodide (24.9

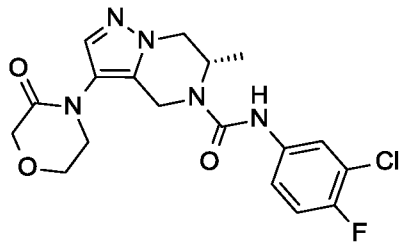
mg, 150 μmol), and 2-bromopyrimidine (17.5 mg, 110 μmol). The reaction mixture was stirred at 60°C for 3 hours. The reaction mixture was then cooled down, poured into ice-water and extracted with EtOAc twice. The organic layers were combined and concentrated to give crude compound **363c** (28 mg). LCMS ($M+H^+$): 428.

Step 3: preparation of (6S)-6-methyl-3-[4-[methyl(pyrimidin-2-yl)amino]-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 363)

A solution of (6S)-tert-butyl 6-methyl-3-(4-(methyl(pyrimidin-2-yl)amino)-2-oxopyrrolidin-1-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **363c**, 70 mg, 164 μmol) in trifluoroacetic acid (2 mL) and DCM (1 mL) was stirred at room temperature for 1 hour. The reaction mixture was concentrated. The residue was dissolved in DCE (2 mL), to which was added DIPEA (371 mg, 0.5 mL, 2.87 mmol), and phenyl (3,4,5-trifluorophenyl)carbamate (compound **233c**, 56.9 mg, 213 μmol). The reaction mixture was stirred at 50°C for 2 hours. The reaction mixture was cooled down, washed with ice-water, extracted with DCM twice. The organic layers were combined and concentrated. The residue was purified by prep-HPLC separation to give **Example 363** (28 mg). LCMS ($M+H^+$): 501. ^1H NMR (400MHz, CD_3OD) δ ppm 8.41-8.37 (m, 2H), 7.67 (s, 1H), 7.39 - 7.23 (m, 2H), 6.69-6.64 (m, 1H), 5.65 - 5.47 (m, 1H), 5.12-5.04 (m, 1H), 5.01 - 4.93 (m, 1H), 4.54 (d, *J*=17.0 Hz, 1H), 4.35-4.27 (m, 1H), 4.25 - 4.12 (m, 2H), 3.96-3.87 (m, 1H), 3.22 (s, 3H), 2.97-2.88 (m, 1H), 2.82-2.72 (m, 1H), 1.33-1.26 (m, 3H).

Example 364:

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



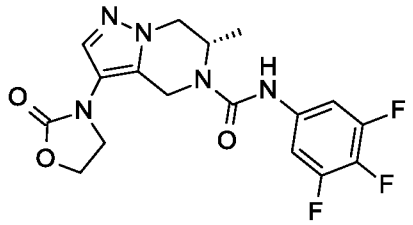
Preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 364):

The title compound was prepared in analogy to the preparation of Example **223** by using morpholin-3-one instead of pyrrolidin-2-one, and phenyl N-(3-chloro-4-fluoro-phenyl)carbamate

(compound **12i**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**).. **Example 364** was obtained as a solid (35 mg). LCMS ($M+H^+$): 408. ^1H NMR (400MHz, chloroform-d) δ ppm 7.62 (dd, *J*=2.8, 6.5 Hz, 1H), 7.52 (s, 1H), 7.49 - 7.41 (m, 1H), 7.28 - 7.25 (m, 1H), 7.06 (t, *J*=8.8 Hz, 1H), 5.15 - 5.03 (m, 1H), 4.89 (d, *J*=16.6 Hz, 1H), 4.38 (s, 2H), 4.36 - 4.26 (m, 2H), 4.15 - 4.00 (m, 3H), 3.97 - 3.90 (m, 1H), 3.74 (ddd, *J*=4.0, 5.8, 12.0 Hz, 1H), 1.36 (d, *J*=7.0 Hz, 3H).

Example 365:

(6S)-6-methyl-3-(2-oxooxazolidin-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

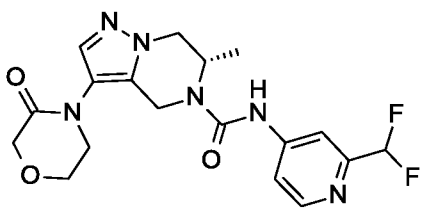


Preparation of (6S)-6-methyl-3-(2-oxooxazolidin-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 365):

The title compound was prepared in analogy to the preparation of Example **223** by using oxazolidin-2-one instead of pyrrolidin-2-one, and phenyl N-(3,4,5-trifluoropheny)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 365** was obtained as a solid (30 mg). LCMS ($M+H^+$): 396. ^1H NMR (400MHz, chloroform-d) δ ppm 7.46 (s, 1H), 7.29 (s, 1H), 7.18 (dd, *J*=6.3, 9.8 Hz, 2H), 5.15 - 5.01 (m, 2H), 4.67 - 4.54 (m, 2H), 4.46 (d, *J*=16.8 Hz, 1H), 4.27 (dd, *J*=5.3, 12.8 Hz, 1H), 4.19 - 3.97 (m, 3H), 1.33 (d, *J*=7.0 Hz, 3H).

Example 366:

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-6-methyl-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

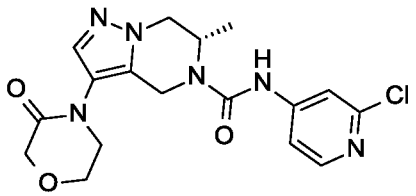


Preparation of (6S)-N-[2-(difluoromethyl)-4-pyridyl]-6-methyl-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 366):

The title compound was prepared in analogy to Example **223** by using morpholin-3-one instead of pyrrolidin-2-one. **Example 366** was obtained as a solid (14 mg). LCMS ($M+H^+$): 407. ^1H NMR (400MHz, chloroform-d) δ ppm 8.48 (d, *J*=5.5 Hz, 1H), 8.23 (s, 1H), 7.79 (d, *J*=1.8 Hz, 1H), 7.67 - 7.60 (m, 1H), 7.53 (s, 1H), 6.75 - 6.45 (m, 1H), 5.17 - 5.04 (m, 1H), 4.96 (d, *J*=17.1 Hz, 1H), 4.41 (s, 2H), 4.37 - 4.31 (m, 2H), 4.15 - 4.03 (m, 3H), 4.02 - 3.95 (m, 1H), 3.74 (ddd, *J*=3.6, 5.6, 11.8 Hz, 1H), 1.43 (d, *J*=7.0 Hz, 3H).

Example 367:

(6S)-N-(2-chloro-4-pyridyl)-6-methyl-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

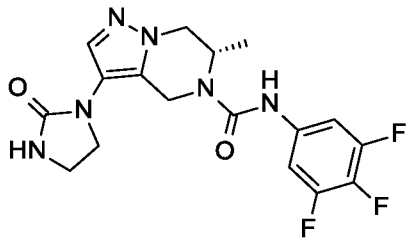


Preparation of (6S)-N-(2-chloro-4-pyridyl)-6-methyl-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 367):

The title compound was prepared in analogy to the preparation of Example **223** by using morpholin-3-one instead of pyrrolidin-2-one, and N-(2-chloro-4-pyridyl)carbamate instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 367** was obtained as a solid (41 mg). LCMS ($M+H^+$): 391. ^1H NMR (400MHz, chloroform-d) δ ppm 8.31 - 8.13 (m, 2H), 7.61 (d, *J*=1.8 Hz, 1H), 7.52 (s, 1H), 7.38 (dd, *J*=1.9, 5.6 Hz, 1H), 5.14 - 5.03 (m, 1H), 4.94 (d, *J*=17.1 Hz, 1H), 4.40 (s, 2H), 4.36 - 4.26 (m, 2H), 4.15 - 3.93 (m, 4H), 3.73 (ddd, *J*=3.6, 5.7, 12.0 Hz, 1H), 1.43 (d, *J*=7.0 Hz, 3H).

Example 368:

(6S)-6-methyl-3-(2-oxoimidazolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

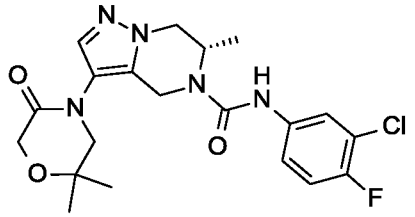


Preparation of (6S)-6-methyl-3-(2-oxoimidazolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 368):

The title compound was prepared in analogy to the preparation of Example **223** by using imidazolidin-2-one instead of pyrrolidin-2-one, and phenyl N-(3,4,5-trifluorophenyl)carbamate (compound **223c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 368** was obtained as a solid (20 mg). LCMS ($M+H^+$): 395. ^1H NMR (400MHz, chloroform-d) δ ppm 8.16 (s, 1H), 7.39 (s, 1H), 7.28 - 7.22 (m, 2H), 5.15 (d, *J*=17.1 Hz, 1H), 5.10 - 5.01 (m, 1H), 4.69 - 4.63 (m, 1H), 4.34 (d, *J*=16.8 Hz, 1H), 4.31 - 4.24 (m, 1H), 4.09 - 4.01 (m, 1H), 4.01 - 3.95 (m, 1H), 3.89 - 3.80 (m, 1H), 3.71 - 3.64 (m, 2H), 1.42 (d, *J*=7.0 Hz, 3H).

Example 371:

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(2,2-dimethyl-5-oxo-morpholin-4-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

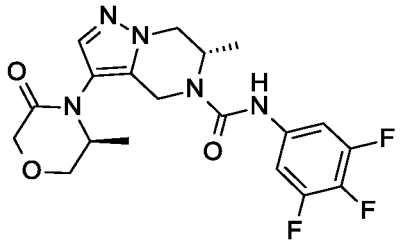


Preparation of (6S)-N-(3-chloro-4-fluoro-phenyl)-3-(2,2-dimethyl-5-oxo-morpholin-4-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 371):

The title compound was prepared in analogy to **Example 223** by using 6,6-dimethylmorpholin-3-one instead of pyrrolidin-2-one, phenyl N-(3-chloro-4-fluoro-phenyl)carbamate (compound **12i**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 371** was obtained as a solid (4 mg). LCMS ($M+H^+$): 436. ^1H NMR (400MHz, CD_3OD) δ ppm 7.63 (s, 2H), 7.37 - 7.31 (m, 1H), 7.18 (s, 1H), 5.03 - 4.92 (m, 2H), 4.46 - 4.38 (m, 1H), 4.31 (s, 3H), 4.20 - 4.14 (m, 1H), 3.72 - 3.63 (m, 2H), 1.43 (d, *J*=3.0 Hz, 6H), 1.28 (d, *J*=7.0 Hz, 3H).

Example 372:

(6S)-6-methyl-3-[(3S)-3-methyl-5-oxo-morpholin-4-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

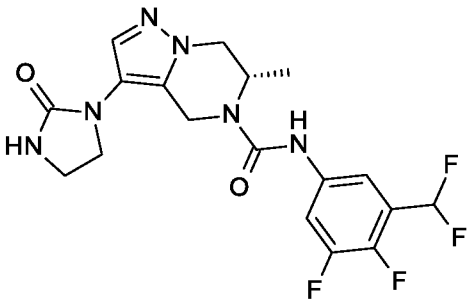


Preparation of (6S)-6-methyl-3-[(3S)-3-methyl-5-oxo-morpholin-4-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 372):

The title compound was prepared in analogy to **Example 223** by using (5S)-5-methylmorpholin-3-one instead of pyrrolidin-2-one, and phenyl N-(3,4,5-trifluorophenyl)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 372** was obtained as a solid (14 mg). LCMS ($M+H^+$): 424. ^{1}H NMR (400MHz, chloroform-d) δ ppm 7.91 (s, 1H), 7.49 (s, 1H), 7.25 (dd, *J*=6.3, 9.8 Hz, 2H), 5.12 (quin, *J*=6.6 Hz, 1H), 4.84 (d, *J*=16.8 Hz, 1H), 4.38 (d, *J*=4.5 Hz, 2H), 4.32 - 4.25 (m, 1H), 4.18 (d, *J*=17.1 Hz, 2H), 4.05 (s, 2H), 3.86 - 3.79 (m, 1H), 1.40 (d, *J*=7.0 Hz, 3H), 1.25 (d, *J*=6.5 Hz, 3H).

Example 373:

(6S)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-6-methyl-3-(2-oxoimidazolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

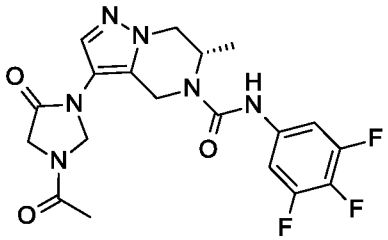


Preparation of (6S)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-6-methyl-3-(2-oxoimidazolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 373):

The title compound was prepared in analogy to the preparation of Example **223** by using imidazolidin-2-one instead of pyrrolidin-2-one, and phenyl N-[3-(difluoromethyl)-4,5-difluoro-phenyl]carbamate (compound **239a**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 373** was obtained as a solid (4 mg). LCMS ($M+H^+$): 427. ^1H NMR (400MHz, chloroform-d) δ ppm 8.16 - 8.07 (m, 1H), 7.78 - 7.68 (m, 1H), 7.45 - 7.37 (m, 2H), 6.84 (s, 1H), 5.16 (d, *J*=16.8 Hz, 1H), 5.10 - 5.00 (m, 1H), 4.81 - 4.72 (m, 1H), 4.45 - 4.34 (m, 1H), 4.33 - 4.24 (m, 1H), 4.08 - 3.97 (m, 2H), 3.90 - 3.79 (m, 1H), 3.70 - 3.62 (m, 2H), 1.40 (d, *J*=7.0 Hz, 3H).

Example 374:

(6S)-3-(3-acetyl-5-oxo-imidazolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

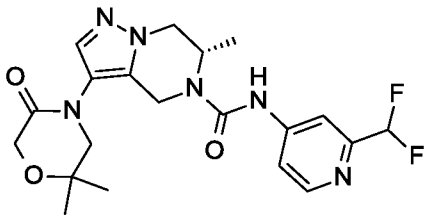


Preparation of (6S)-3-(3-acetyl-5-oxo-imidazolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 374)

The title compound was prepared in analogy to **Example 248** by using acetyl chloride instead of methylsulfonyl methanesulfonate. **Example 374** was obtained as a white solid (41 mg). LCMS ($M+H^+$): 427. ^1H NMR (400MHz, chloroform-d) δ ppm 7.73 (s, 1H), 7.57 - 7.47 (m, 1H), 7.27 - 7.16 (m, 2H), 5.39 - 5.28 (m, 1H), 5.26 - 5.15 (m, 1H), 5.12 - 4.99 (m, 2H), 4.42 (d, *J*=16.8 Hz, 1H), 4.35 - 4.21 (m, 3H), 4.08 (dd, *J*=1.6, 12.9 Hz, 1H), 2.24 - 2.12 (m, 3H), 1.40 - 1.30 (m, 3H).

Example 375:

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-3-(2,2-dimethyl-5-oxo-morpholin-4-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

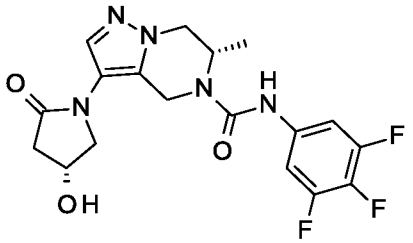


Preparation of (6S)-N-[2-(difluoromethyl)-4-pyridyl]-3-(2,2-dimethyl-5-oxo-morpholin-4-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 375):

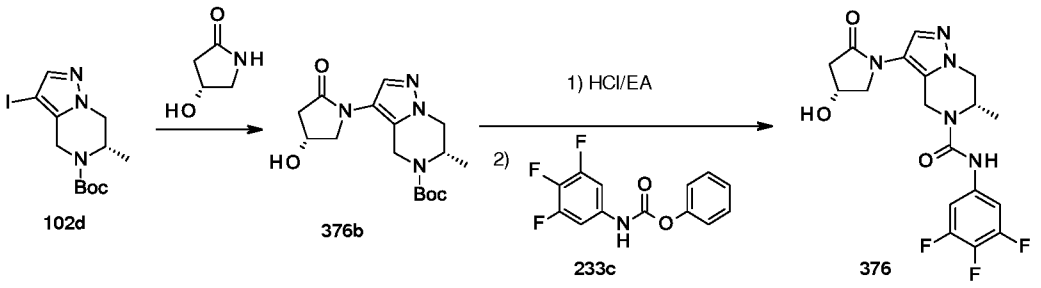
The title compound was prepared in analogy to **Example 223** by using 6,6-dimethylmorpholin-3-one instead of pyrrolidin-2-one. **Example 375** was obtained as a solid (34 mg). LCMS ($M+H^+$): 435. ^1H NMR (400MHz, chloroform-d) δ ppm 8.46 (d, *J*=5.8 Hz, 1H), 8.36 (s, 1H), 8.12 (br. s., 1H), 7.79 (d, *J*=2.0 Hz, 1H), 7.65 (dd, *J*=1.9, 5.6 Hz, 1H), 7.51 - 7.43 (m, 1H), 6.78 - 6.44 (m, 1H), 5.15 - 5.03 (m, 1H), 4.97 (d, *J*=16.8 Hz, 1H), 4.44 - 4.26 (m, 4H), 4.06 (dd, *J*=1.5, 13.1 Hz, 1H), 3.73 (d, *J*=12.0 Hz, 1H), 3.55 (d, *J*=12.3 Hz, 1H), 1.44 (d, *J*=8.5 Hz, 6H), 1.37 (d, *J*=7.0 Hz, 3H).

Example 376:

(6S)-3-[(4R)-4-hydroxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:

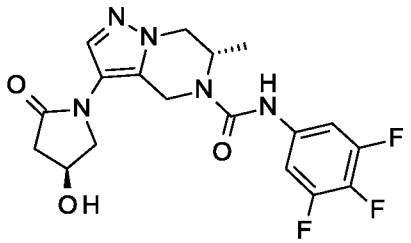


Preparation of (6S)-3-[(4R)-4-hydroxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 376):

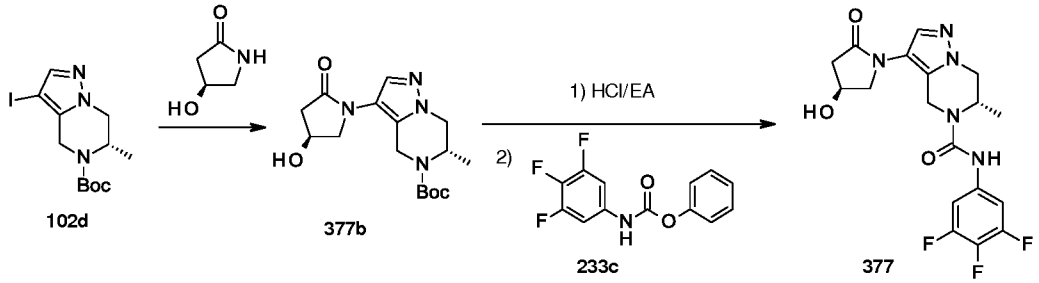
The title compound was prepared in analogy to **Example 223** by using (4R)-4-hydroxypyrrolidin-2-one instead of pyrrolidin-2-one, and phenyl N-(3,4,5-trifluorophenyl)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 376** was obtained as a solid (26 mg). LCMS ($M+H^+$): 410. ^1H NMR (400MHz, chloroform-d) δ ppm 8.02 - 7.92 (m, 1H), 7.44 (s, 1H), 7.27 - 7.16 (m, 2H), 5.14 - 5.05 (m, 1H), 5.01 (d, *J*=16.8 Hz, 1H), 4.72 (t, *J*=6.0 Hz, 1H), 4.45 (d, *J*=16.8 Hz, 1H), 4.31 (dd, *J*=5.4, 12.9 Hz, 1H), 4.10 - 4.01 (m, 2H), 3.80 (dd, *J*=2.1, 10.9 Hz, 1H), 2.91 (dd, *J*=6.5, 17.6 Hz, 1H), 2.57 (dd, *J*=2.5, 17.6 Hz, 1H), 1.37 (d, *J*=7.0 Hz, 3H).

Example 377:

(6S)-3-[(4S)-4-hydroxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:

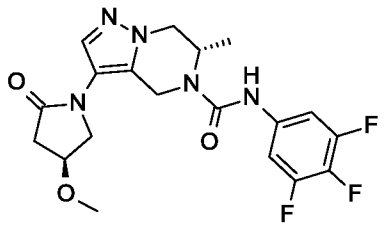


Preparation of (6S)-3-[(4S)-4-hydroxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 377):

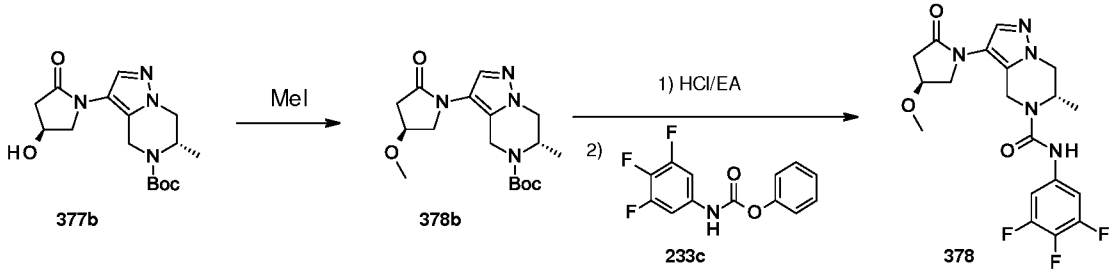
The title compound was prepared in analogy to **Example 223** by using (4S)-4-hydroxypyrrolidin-2-one instead of pyrrolidin-2-one, and phenyl N-(3,4,5-trifluorophenyl)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 377** was obtained as a solid (15 mg). LCMS ($M+H^+$): 410. ^1H NMR (400MHz, chloroform-d) δ ppm 8.07 (s, 1H), 7.41 (s, 1H), 7.23 (dd, *J*=6.3, 9.8 Hz, 2H), 5.19 (d, *J*=16.8 Hz, 1H), 5.08 (t, *J*=7.2 Hz, 1H), 4.75 (t, *J*=5.4 Hz, 1H), 4.38 - 4.18 (m, 3H), 4.02 (dd, *J*=2.0, 13.1 Hz, 1H), 3.68 (d, *J*=10.8 Hz, 1H), 2.95 (dd, *J*=6.1, 17.7 Hz, 1H), 2.62 (d, *J*=18.1 Hz, 1H), 2.38 (br. s., 1H), 1.38 (d, *J*=7.0 Hz, 3H).

Example 378:

(6S)-3-[(4S)-4-methoxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: **preparation of (S)-tert-butyl 3-((S)-4-methoxy-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 378b)**

To a solution of compound (S)-tert-butyl 3-((S)-4-hydroxy-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **377b**, 336 mg, 1 mmol) in acetonitrile (5 mL) was added Ag_2O (695 mg, 3 mmol), triethylamine (101 mg, 139 μL, 1 mmol) and iodomethane (4.26 g, 30 mmol). The reaction mixture was flushed with nitrogen and stirred at 80°C in microwave for 25 minutes. The reaction mixture was filtrated and concentrated. The residue was purified by silica gel column to give compound **378b** (175 mg). LCMS ($M+H^+$): 351.

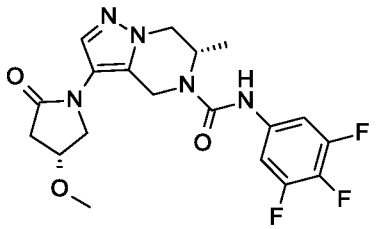
Step 2: preparation of (6S)-3-[(4S)-4-methoxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 378)

mixture solution of compound (S)-tert-butyl 3-((S)-4-methoxy-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **378b**, 32 mg, 91.3 μmol) in HCl/EtOAc (ca. 1mol/L, 5 mL, 5 mmol) was stirred at room temperature overnight. The reaction mixture was concentrated. The residue was dissolved in DMF (2 mL), to which was added DIPEA (226 mg, 0.3 mL, 1.75 mmol), phenyl (3,4,5-trifluorophenyl)carbamate (compound **233c**, 29.3 mg, 110 μmol). The reaction mixture was stirred at 40°C for 2 hours, and

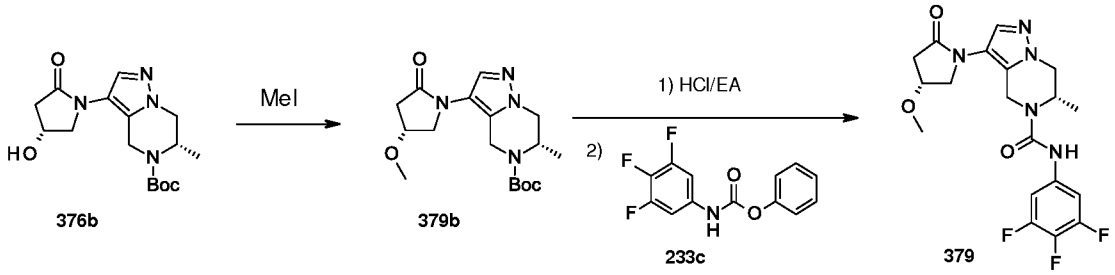
then purified by prep-HPLC to give **Example 378** (20 mg). LCMS ($M+H^+$): 424. ^1H NMR (400MHz, chloroform-d) δ ppm 8.06 (s, 1H), 7.40 (s, 1H), 7.30 (s, 1H), 7.27 (d, *J*=6.3 Hz, 1H), 5.12 (s, 1H), 5.10 - 5.02 (m, 1H), 4.31 (d, *J*=16.6 Hz, 2H), 4.25 - 4.19 (m, 1H), 4.17 - 4.11 (m, 1H), 4.03 - 3.96 (m, 1H), 3.79 - 3.71 (m, 1H), 3.42 (s, 3H), 2.92 - 2.81 (m, 1H), 2.74 - 2.65 (m, 1H), 1.40 (d, *J*=7.0 Hz, 3H).

Example 379:

(6S)-3-[(4R)-4-methoxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:

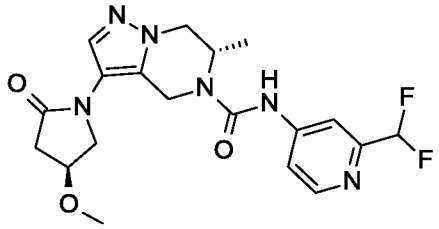


Preparation of (6S)-3-[(4R)-4-methoxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 379)

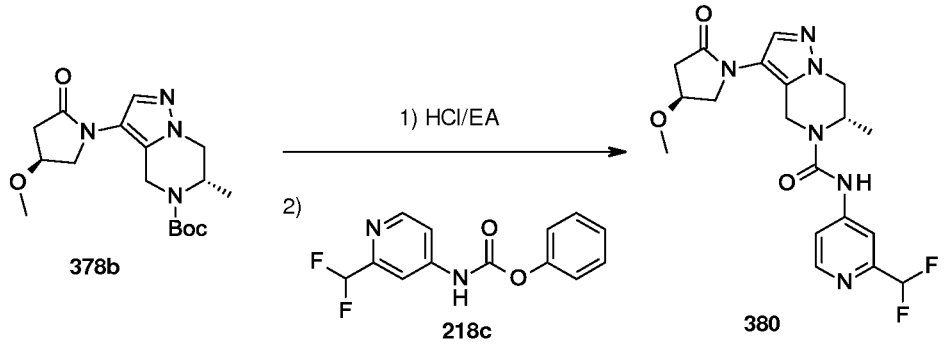
The title compound was prepared in analogy to **Example 378** by using (R)-tert-butyl 3-((R)-4-hydroxy-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **376b**) instead of (S)-tert-butyl 3-((S)-4-hydroxy-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **377b**). **Example 379** was obtained as a solid (39 mg). LCMS ($M+H^+$): 424. ^1H NMR (400MHz, chloroform-d) δ ppm 7.88 (s, 1H), 7.44 (s, 1H), 7.28 - 7.21 (m, 2H), 5.13 - 4.98 (m, 2H), 4.40 (d, *J*=16.6 Hz, 1H), 4.33 - 4.26 (m, 1H), 4.25 - 4.19 (m, 1H), 4.06 - 3.97 (m, 2H), 3.90 - 3.84 (m, 1H), 3.43 (s, 3H), 2.90 - 2.81 (m, 1H), 2.73 - 2.64 (m, 1H), 1.39 (d, *J*=6.8 Hz, 3H).

Example 380:

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-3-[(4S)-4-methoxy-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:

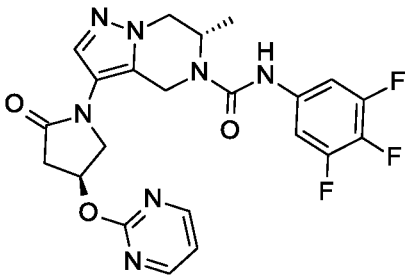


Preparation of (6S)-N-[2-(difluoromethyl)-4-pyridyl]-3-[(4S)-4-methoxy-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 380):

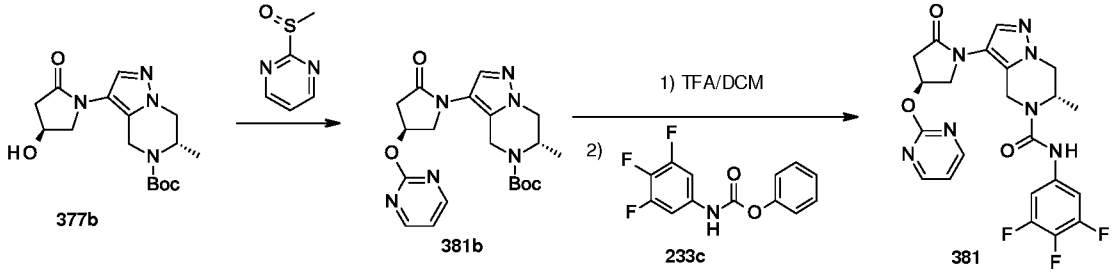
The title compound was prepared in analogy to the preparation of **Example 378** by using phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**) instead of phenyl (3,4,5-trifluorophenyl)carbamate (compound **233c**). **Example 380** was obtained as a solid (19 mg). LCMS ($M+H^+$): 421. ^{1}H NMR (400MHz, chloroform-d) δ ppm 8.47 (d, *J*=4.3 Hz, 2H), 7.83 (s, 1H), 7.66 (d, *J*=5.0 Hz, 1H), 7.40 (s, 1H), 6.59 (s, 1H), 5.24 (d, *J*=17.1 Hz, 1H), 5.08 (br. s., 1H), 4.40 - 4.28 (m, 2H), 4.25 - 4.18 (m, 1H), 4.17 - 4.11 (m, 1H), 4.02 (dd, *J*=2.0, 13.1 Hz, 1H), 3.76 (d, *J*=10.8 Hz, 1H), 3.42 (s, 3H), 2.86 (dd, *J*=6.3, 17.8 Hz, 1H), 2.79 - 2.63 (m, 1H), 1.41 (d, *J*=7.0 Hz, 3H).

Example 381:

(6S)-6-methyl-3-[(4S)-2-oxo-4-pyrimidin-2-yloxy-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: **preparation of (S)-tert-butyl 6-methyl-3-((S)-2-oxo-4-(pyrimidin-2-yloxy)pyrrolidin-1-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 381b)**

The reaction mixture of compound (S)-tert-butyl 3-((S)-4-hydroxy-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **377b**, 67.3 mg, 0.2 mmol) and 2-(methylsulfinyl)pyrimidine (114 mg, 800 μmol) in dry acetonitrile (2 mL) was refluxed for 10 minutes, then to which was added K_2CO_3 (55.3 mg, 400 μmol). The reaction mixture was stirred at 85 °C for 5 hours. The reaction mixture was diluted with EtOAc, and centrifuged. The organic phase was separated and concentrated. The residue was purified by silica gel column to give compound **381b** (50 mg). LCMS ($M+H^+$): 415.

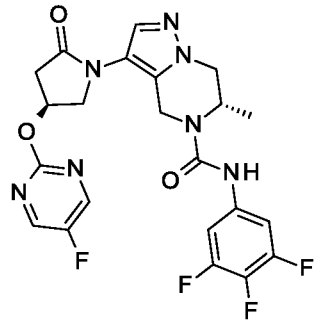
Step 2: preparation of (6S)-6-methyl-3-[(4S)-2-oxo-4-pyrimidin-2-yloxy-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 381)

A solution of compound (S)-tert-butyl 6-methyl-3-((S)-2-oxo-4-(pyrimidin-2-yloxy)pyrrolidin-1-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **381b**, 100 mg, 241 μmol) in trifluoroacetic acid (2 mL) and DCM (1 mL) was stirred at room temperature for 1 hour. The reaction mixture was concentrated. The residue was dissolved in DCE (2 mL) , to which was added DIPEA (371 mg, 0.5 mL, 2.87 mmol), and phenyl (3,4,5-trifluorophenyl)carbamate (compound **233c**, 83.8 mg, 314 μmol). The reaction mixture was stirred at 50°C for 2 hours, and then concentrated. the residue was purified first by silica gel column and then prep-HPLC to give **Example 381** (50 mg). LCMS ($M+H^+$): 488. ^1H NMR

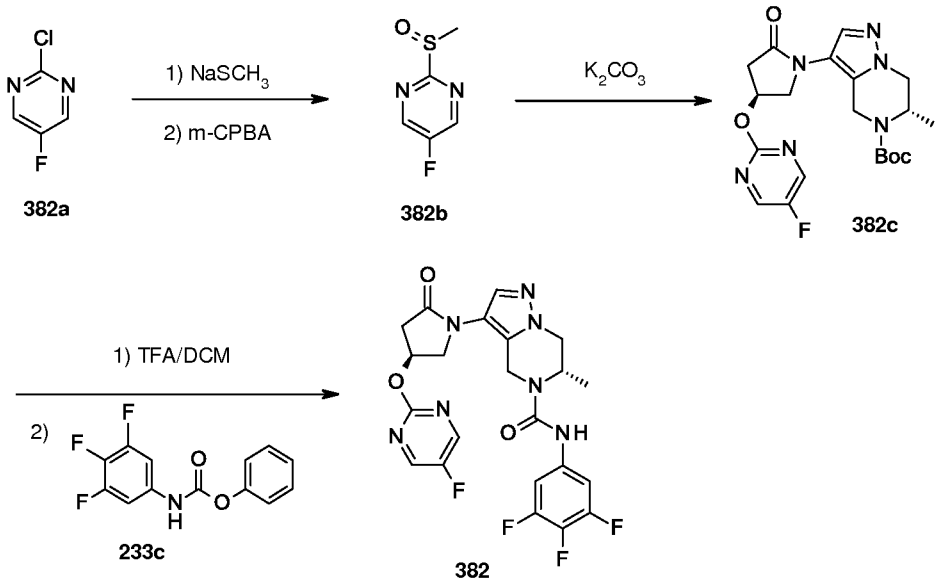
(400MHz, chloroform-d) δ ppm 8.63 (d, *J*=4.8 Hz, 2H), 7.65 (s, 1H), 7.38 - 7.23 (m, 2H), 7.18 (s, 1H), 5.78 (dt, *J*=1.7, 5.3 Hz, 1H), 5.09 (d, *J*=16.9 Hz, 1H), 5.03 - 4.93 (m, 1H), 4.55 - 4.46 (m, 1H), 4.42 - 4.35 (m, 1H), 4.34 - 4.26 (m, 1H), 4.18 (s, 1H), 3.99 (d, *J*=1.2 Hz, 1H), 3.24 - 3.12 (m, 1H), 2.82 - 2.69 (m, 1H), 1.26 (d, *J*=6.8 Hz, 3H).

Example 382:

(6S)-3-[(4S)-4-(5-fluoropyrimidin-2-yl)oxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: **preparation of 5-fluoro-2-(methylsulfinyl)pyrimidine (compound 382b)**

To a solution of 2-chloro-5-fluoropyrimidine (compound **382a**, 398 mg, 3 mmol) in DMF (6 mL) at 5°C was added dropwise sodium thiomethoxide (1.26 g, 1.15 mL, 2.7 mmol) (ca. 15% in water). The reaction mixture was stirred at 5°C for 1 hour, then diluted with mixed solvent of PE/EtOAc (v/v=5/1), and washed with water. The organic phase was separated and concentrated to give crude intermediate 5-fluoro-2-methylsulfanyl-pyrimidine. The intermediate was dissolved in DCM (6 mL), then to which was added 3-chloroperoxybenzoic acid (*m*-CPBA) (518

mg, 3 mmol). The reaction mixture was stirred at room temperature for 2 hours, and then purified by silica gel column to give compound **382b** (160 mg). LCMS ($M+H^+$): 161.

Step 2: **preparation of (S)-tert-butyl 3-((S)-4-((5-fluoropyrimidin-2-yl)oxy)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 382c)**

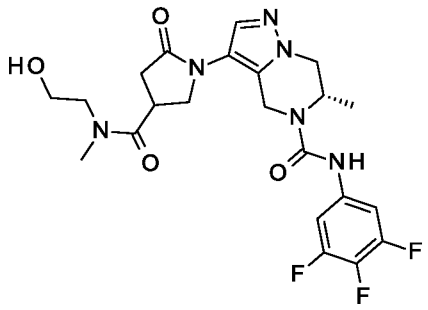
Compound **382c** was prepared in analogy to compound **381b** by using 5-fluoro-2-(methylsulfinyl)pyrimidine (compound **382b**) instead of 2-(methylsulfinyl)pyrimidine. Compound 382c was obtained as a solid (108 mg). LCMS ($M+H^+$): 433.

Step 3: preparation of (6S)-3-[(4S)-4-(5-fluoropyrimidin-2-yl)oxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 382)

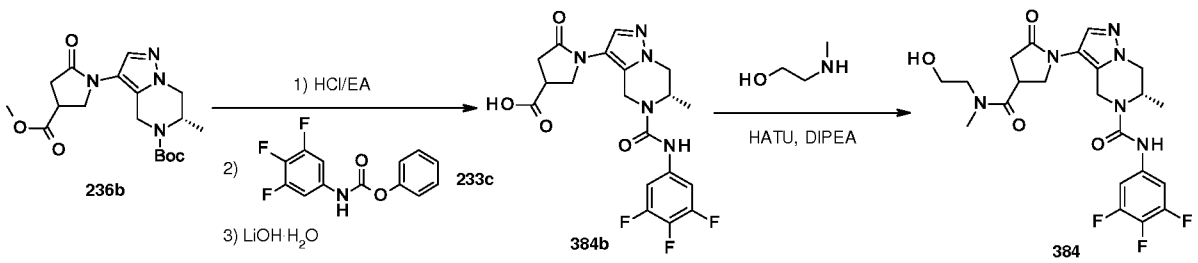
The title compound was prepared in analogy to the preparation of **Example 381** by using (S)-tert-butyl 3-((S)-4-((5-fluoropyrimidin-2-yl)oxy)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **382c**) instead of (S)-tert-butyl 6-methyl-3-((S)-2-oxo-4-(pyrimidin-2-yloxy)pyrrolidin-1-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **381b**) to give **Example 382** (77 mg). LCMS ($M+H^+$): 506. ^1H NMR (400MHz, CD_3OD) δ ppm 8.58 (s, 2H), 7.65 (s, 1H), 7.37 - 7.18 (m, 2H), 5.75 - 5.68 (m, 1H), 5.09 (d, *J*=16.9 Hz, 1H), 5.01 - 4.93 (m, 1H), 4.50 (d, *J*=16.9 Hz, 1H), 4.42 - 4.34 (m, 1H), 4.33 - 4.27 (m, 1H), 4.22 - 4.11 (m, 1H), 4.02 - 3.94 (m, 1H), 3.17 (dd, *J*=6.8, 18.1 Hz, 1H), 2.74 (dd, *J*=1.8, 18.0 Hz, 1H), 1.26 (d, *J*=6.8 Hz, 3H).

Example 384:

(6S)-3-[4-[2-hydroxyethyl(methyl)carbamoyl]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of 1-((S)-6-methyl-5-((3,4,5-trifluorophenyl)carbamoyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)-5-oxopyrrolidine-3-carboxylic acid (compound 384b)

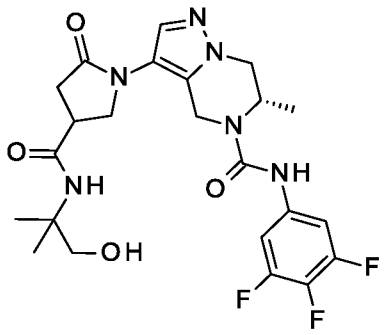
The compound **384b** was prepared in analogy to the preparation of compound **236d** by using phenyl N-(3,4,5-trifluorophenyl)carbamate (compound **233c**) instead of phenyl N-(3-chloro-4-fluoro-phenyl)carbamate (compound **12i**). LCMS ($M+H^+$): 438.

Preparation of (6S)-3-[4-[2-hydroxyethyl(methyl)carbamoyl]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 384)

To a solution of 1-((S)-6-methyl-5-((3,4,5-trifluorophenyl)carbamoyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)-5-oxopyrrolidine-3-carboxylic acid (compound **384b**, 122 mg, 0.28 mmol) in DMF (2 mL) was added 2-(methylamino)ethanol (42.1 mg, 44.8 μL, 560 μmol), DIPEA (151 mg, 0.2 mL, 1.17 mmol) and HATU (128 mg, 336 μmol) sequentially. The reaction mixture was stirred at room temperature overnight, and then purified by prep-HPLC to give **Example 384** (13 mg). LCMS ($M+H^+$): 495. ^1H NMR (400MHz, CD_3OD) δ ppm 7.64 (d, *J*=4.3 Hz, 1H), 7.36 - 7.24 (m, 2H), 5.04 (d, *J*=16.8 Hz, 2H), 4.56 - 4.48 (m, 1H), 4.33 - 4.26 (m, 1H), 4.18 (s, 1H), 4.13 - 3.83 (m, 3H), 3.74 (d, *J*=5.5 Hz, 2H), 3.67 - 3.50 (m, 2H), 3.23 - 3.01 (m, 3H), 2.80 (s, 2H), 1.26 (d, *J*=7.0 Hz, 3H).

Example 385:

(6S)-3-[4-[(2-hydroxy-1,1-dimethyl-ethyl)carbamoyl]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

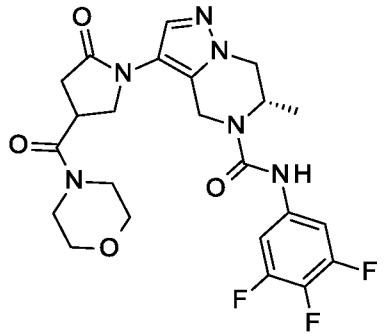


Preparation of (6S)-3-[4-[(2-hydroxy-1,1-dimethyl-ethyl)carbamoyl]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 385):

The title compound was prepared in analogy to **Example 384** by using 2-amino-2-methylpropan-1-ol instead of 2-(methylamino)ethanol. **Example 385** was obtained as a white solid (16 mg). LCMS (M+H+): 509. ^{1}H NMR (400MHz, MeOD) δ ppm 7.64 (s, 1H), 7.30 (dd, *J*=6.3, 10.3 Hz, 2H), 5.04 (d, *J*=16.8 Hz, 1H), 5.00 - 4.93 (m, 1H), 4.52 (d, *J*=16.8 Hz, 1H), 4.33 - 4.25 (m, 1H), 4.18 (s, 1H), 3.99 (d, *J*=8.8 Hz, 1H), 3.92 (d, *J*=5.5 Hz, 1H), 3.65 (d, *J*=6.0 Hz, 2H), 3.42 - 3.35 (m, 1H), 2.84 - 2.69 (m, 2H), 1.33 - 1.24 (m, 9H).

Example 386:

(6S)-6-methyl-3-[4-(morpholine-4-carbonyl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



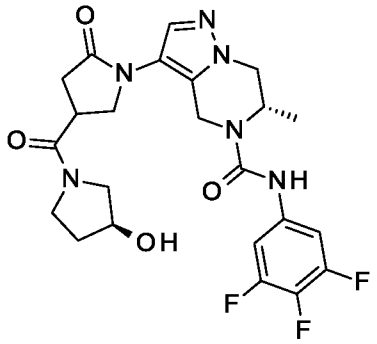
Preparation of (6S)-6-methyl-3-[4-(morpholine-4-carbonyl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 386):

The title compound was prepared in analogy to **Example 384** by using morpholine instead of 2-(methylamino)ethanol. **Example 386** was obtained as a white solid (20 mg). LCMS (M+H+): 507. ^{1}H NMR (400MHz, MeOD) δ ppm 7.65 (s, 1H), 7.35 - 7.23 (m, 2H), 5.04 (d,

J=17.1 Hz, 2H), 4.50 (d, *J*=16.8 Hz, 1H), 4.35 - 4.26 (m, 1H), 4.19 - 3.92 (m, 3H), 3.89 - 3.79 (m, 1H), 3.75 - 3.60 (m, 8H), 2.93 - 2.75 (m, 2H), 1.30 - 1.23 (m, 3H).

Example 387:

(6S)-3-[4-[(3S)-3-hydroxypyrrolidine-1-carbonyl]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

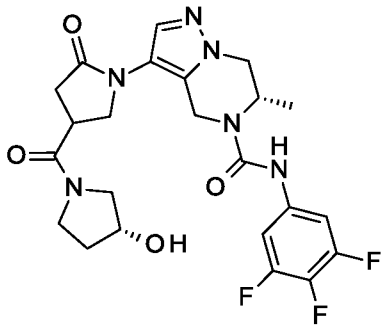


Preparation of (6S)-3-[4-[(3S)-3-hydroxypyrrolidine-1-carbonyl]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 387):

The title compound was prepared in analogy to **Example 384** by using (S)-pyrrolidin-3-ol instead of 2-(methylamino)ethanol. **Example 387** was obtained as a white solid (35 mg). LCMS (M+H+): 507. ^{1}H NMR (400MHz, MeOD) δ ppm 7.66 (s, 0.5H), 7.65 (s, 0.5H), 7.36-7.25 (m, 2H), 5.10 - 4.94 (m, 2H), 4.58 - 4.42 (m, 2H), 4.33 - 4.26 (m, 1H), 4.19 - 4.06 (m, 2H), 4.01 - 3.88 (m, 1H), 3.78 - 3.48 (m, 5H), 2.94 - 2.74 (m, 2H), 2.20 - 1.93 (m, 2H), 1.30-1.24 (m, 3H).

Example 388:

(6S)-3-[4-[(3R)-3-hydroxypyrrolidine-1-carbonyl]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

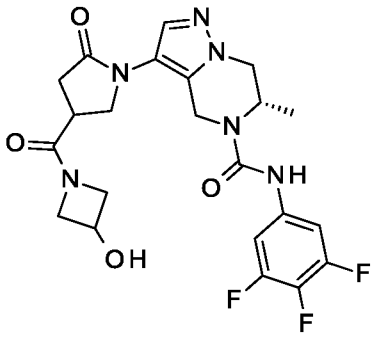


Preparation of (6S)-3-[4-[(3R)-3-hydroxypyrrolidine-1-carbonyl]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 388):

The title compound was prepared in analogy to **Example 384** by using (R)-pyrrolidin-3-ol instead of 2-(methylamino)ethanol. **Example 388** was obtained as a white solid (15 mg). LCMS (M+H+): 507. ^{1}H NMR (400MHz, MeOD) δ ppm 7.66 (s, 0.5H), 7.65 (s, 0.5H), 7.35 - 7.26 (m, 2H), 5.08 - 4.96 (m, 2H), 4.56 - 4.43 (m, 2H), 4.34 - 4.26 (m, 1H), 4.19 - 4.03 (m, 2H), 4.00 - 3.90 (m, 1H), 3.79 - 3.47 (m, 5H), 2.94 - 2.74 (m, 2H), 2.20 - 1.94 (m, 2H), 1.30-1.24 (m, 3H).

Example 389:

(6S)-3-[4-(3-hydroxyazetidine-1-carbonyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

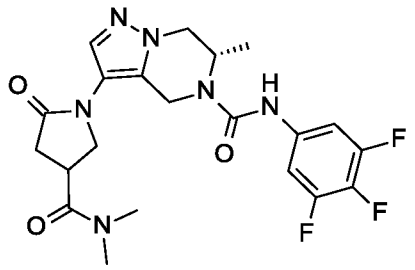


Preparation of (6S)-3-[4-(3-hydroxyazetidine-1-carbonyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 389):

The title compound was prepared in analogy to **Example 384** by using azetidin-3-ol instead of 2-(methylamino)ethanol. **Example 389** was obtained as a white solid (16 mg). LCMS (M+H+): 493. ^{1}H NMR (400MHz, MeOD) δ ppm 7.64 (s, 0.5H), 7.64 (s, 0.5H),, 7.34 - 7.25 (m, 2H), 5.07 - 4.94 (m, 2H), 4.67 - 4.59 (m, 1H), 4.55 - 4.47 (m, 2H), 4.33 - 4.22 (m, 2H), 4.19 - 4.13 (m, 1H), 4.11 - 3.98 (m, 2H), 3.94 - 3.78 (m, 2H), 3.54 - 3.44 (m, 1H), 2.87 - 2.68 (m, 2H), 1.30-1.24 (m, 3H).

Example 390:

(6S)-3-[4-(dimethylcarbamoyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

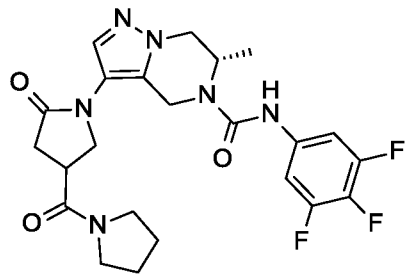


Preparation of (6S)-3-[4-(dimethylcarbamoyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 390):

The title compound was prepared in analogy to **Example 384** by using dimethylamine instead of 2-(methylamino)ethanol. **Example 390** was obtained as a white solid (30 mg). LCMS (M+H+): 465. ^{1}H NMR (400MHz, MeOD) δ ppm 7.64 (s, 1H), 7.35-7.25 (m, 2H), 5.08-4.94 (m, 2H), 4.56 - 4.47 (m, 1H), 4.33 - 4.25 (m, 1H), 4.19-4.03 (m, 2H), 3.99 - 3.81 (m, 2H), 3.16 (s, 3H), 3.01 (s, 3H), 2.92 - 2.82 (m, 1H), 2.80 - 2.72 (m, 1H), 1.30-1.24 (m, 3H).

Example 391:

(6S)-6-methyl-3-[2-oxo-4-(pyrrolidine-1-carbonyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

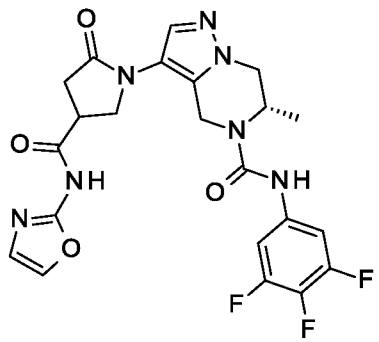


Preparation of (6S)-6-methyl-3-[2-oxo-4-(pyrrolidine-1-carbonyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 391):

The title compound was prepared in analogy to **Example 384** by using pyrrolidine instead of 2-(methylamino)ethanol. **Example 391** was obtained as a white solid (28 mg). LCMS (M+H+): 491. ^{1}H NMR (400MHz, MeOD) δ ppm 7.64 (s, 1H), 7.35 - 7.25 (m, 2H), 5.07 - 4.93 (m, 2H), 4.55 - 4.48 (m, 1H), 4.33 - 4.25 (m, 1H), 4.19 - 4.04 (m, 2H), 3.99 - 3.89 (m, 1H), 3.76 - 3.66 (m, 1H), 3.65-3.56 (m, 2H), 3.51-3.45 (m, 2H), 2.92 - 2.82 (m, 1H), 2.80 - 2.73 (m, 1H), 2.08 - 1.99 (m, 2H), 1.97 - 1.88 (m, 2H), 1.30-1.24 (m, 3H)

Example 392:

(6S)-6-methyl-3-[4-(oxazol-2-ylcarbamoyl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

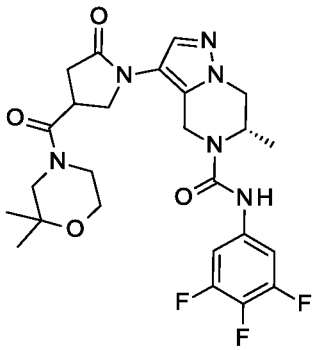


Preparation of (6S)-6-methyl-3-[4-(oxazol-2-ylcarbamoyl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 392):

The title compound was prepared in analogy to **Example 384** by using oxazol-2-amine instead of 2-(methylamino)ethanol. **Example 392** was obtained as a white solid (5 mg). LCMS (M+H+): 504. ^{1}H NMR (400MHz, MeOD) δ ppm 7.70 - 7.60 (m, 2H), 7.35 - 7.25 (m, 2H), 7.10 (s, 1H), 5.08 - 4.94 (m, 2H), 4.55 - 4.46 (m, 1H), 4.28 (d, *J*=4.5 Hz, 1H), 4.20 - 3.99 (m, 3H), 3.62 (br. s., 1H), 3.54 - 3.45 (m, 1H), 2.99 - 2.81 (m, 2H), 1.33 - 1.21 (m, 3H).

Example 393:

(6S)-3-[4-(2,2-dimethylmorpholine-4-carbonyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

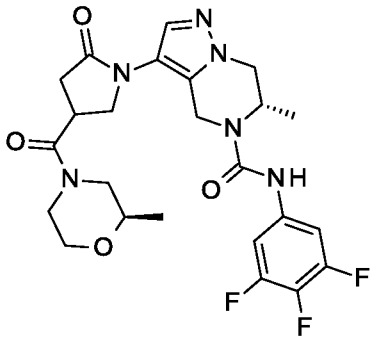


Preparation of (6S)-3-[4-(2,2-dimethylmorpholine-4-carbonyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 393):

The title compound was prepared in analogy to **Example 384** by using 2,2-dimethylmorpholine instead of 2-(methylamino)ethanol. **Example 393** was obtained as a white solid (23 mg). LCMS (M+H+): 535. ^{1}H NMR (400MHz, MeOD) δ ppm 7.64 (s, 1H), 7.34 - 7.25 (m, 2H), 5.07 - 4.95 (m, 2H), 4.54 - 4.47 (m, 1H), 4.33 - 4.27 (m, 1H), 4.16 (d, *J*=12.5 Hz, 1H), 4.12 - 4.05 (m, 1H), 4.02 - 3.93 (m, 1H), 3.91 - 3.74 (m, 3H), 3.65 - 3.57 (m, 2H), 3.52 - 3.44 (m, 2H), 2.81 (d, *J*=6.5 Hz, 2H), 1.30 - 1.19 (m, 9H).

Example 394:

(6S)-6-methyl-3-[4-[(2R)-2-methylmorpholine-4-carbonyl]-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

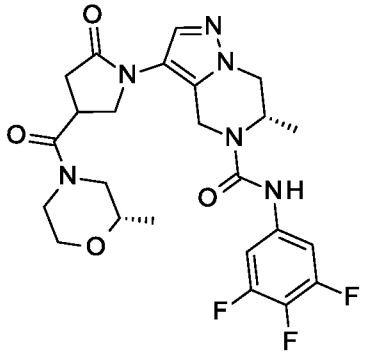


Preparation of (6S)-6-methyl-3-[4-[(2R)-2-methylmorpholine-4-carbonyl]-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 394):

The title compound was prepared in analogy to **Example 384** by using (R)-2-methylmorpholine instead of 2-(methylamino)ethanol. **Example 394** was obtained as a white solid (21 mg). LCMS (M+H+): 521. ^{1}H NMR (400MHz, MeOD) δ ppm 7.66 - 7.62 (m, 1H), 7.34 - 7.25 (m, 2H), 5.09 - 4.94 (m, 2H), 4.56 - 4.46 (m, 1H), 4.42 - 4.35 (m, 1H), 4.34 - 4.27 (m, 1H), 4.17 (s, 1H), 4.12 - 3.83 (m, 5H), 3.54 (br. s., 2H), 3.05 - 2.44 (m, 4H), 1.30 - 1.17 (m, 6H).

Example 395:

(6S)-6-methyl-3-[4-[(2S)-2-methylmorpholine-4-carbonyl]-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

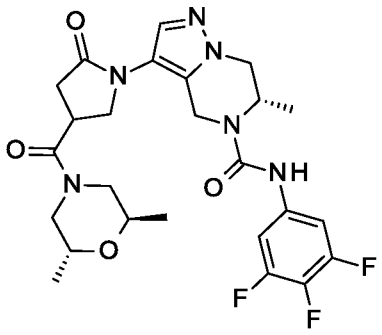


Preparation of (6S)-6-methyl-3-[4-[(2S)-2-methylmorpholine-4-carbonyl]-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 395):

The title compound was prepared in analogy to **Example 384** by using (S)-2-methylmorpholine instead of 2-(methylamino)ethanol. **Example 395** was obtained as a white solid (14 mg). LCMS (M+H+): 521. ^{1}H NMR (400MHz, MeOD) δ ppm 7.66 - 7.62 (m, 1H), 7.34 - 7.25 (m, 2H), 5.07 - 4.93 (m, 2H), 4.55 - 4.46 (m, 1H), 4.41 - 4.26 (m, 2H), 4.18 - 3.83 (m, 6H), 3.64 - 3.48 (m, 2H), 3.02 - 2.49 (m, 4H), 1.31 - 1.18 (m, 6H).

Example 396:

(6S)-3-[4-[trans-2,6-dimethylmorpholine-4-carbonyl]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



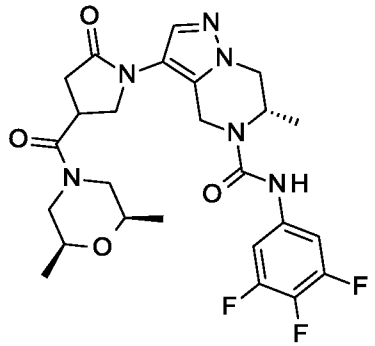
Preparation of (6S)-3-[4-[trans-2,6-dimethylmorpholine-4-carbonyl]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 396):

The title compound was prepared in analogy to **Example 384** by using trans-2,6-dimethylmorpholine instead of 2-(methylamino)ethanol. **Example 396** was obtained as a white solid (20 mg). LCMS (M+H+): 535. ^{1}H NMR (400MHz, MeOD) δ ppm 7.64 (m, 1H), 7.35 - 7.23 (m, 2H), 5.08 - 4.93 (m, 2H), 4.55 - 4.45 (m, 1H), 4.44 - 4.36 (m, 1H), 4.33 - 4.25 (m, 1H),

4.19 - 3.83 (m, 5H), 3.69 - 3.51 (m, 2H), 2.94 - 2.72 (m, 3H), 2.43 (dd, *J*=10.8, 13.1 Hz, 1H), 1.31 - 1.17 (m, 9H).

Example 397:

(6S)-3-[4-[cis-2,6-dimethylmorpholine-4-carbonyl]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

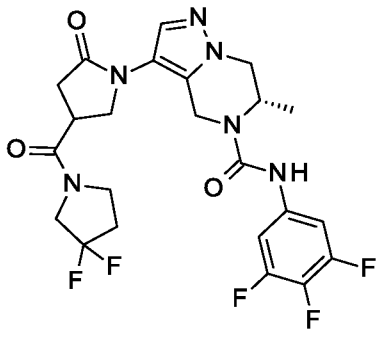


Preparation of (6S)-3-[4-[cis-2,6-dimethylmorpholine-4-carbonyl]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 397):

The title compound was prepared in analogy to **Example 384** by using cis-2,6-dimethylmorpholine instead of 2-(methylamino)ethanol. **Example 397** was obtained as a white solid (24 mg). LCMS (M+H+): 535. ^{1}H NMR (400MHz, MeOD) δ ppm 7.66 - 7.62 (m, 1H), 7.34 - 7.25 (m, 2H), 5.08 - 4.92 (m, 2H), 4.54 - 4.46 (m, 1H), 4.34 - 4.25 (m, 1H), 4.19 - 4.13 (m, 1H), 4.12 - 3.82 (m, 5H), 3.76 - 3.38 (m, 3H), 2.96 - 2.35 (m, 3H), 1.31 - 1.17 (m, 9H).

Example 398:

(6S)-3-[4-(3,3-difluoropyrrolidine-1-carbonyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

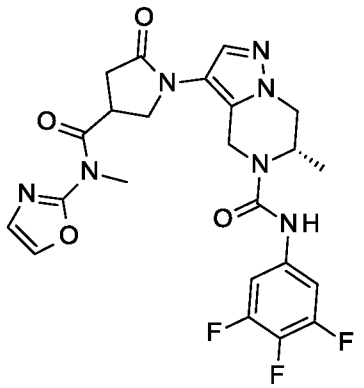


Preparation of (6S)-3-[4-(3,3-difluoropyrrolidine-1-carbonyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 398):

The title compound was prepared in analogy to **Example 384** by using 3,3-difluoropyrrolidine hydrochloride instead of 2-(methylamino)ethanol. **Example 398** was obtained as a white solid (3 mg). LCMS (M+H+): 527. ^{1}H NMR (400MHz, MeOD) δ ppm 7.64 (s, 1H), 7.34 - 7.25 (m, 2H), 5.08 - 4.94 (m, 2H), 4.56 - 4.46 (m, 1H), 4.35 - 4.25 (m, 1H), 4.18 - 3.63 (m, 8H), 2.93 - 2.84 (m, 1H), 2.81 - 2.72 (m, 1H), 2.60 - 2.39 (m, 2H), 1.30 - 1.24 (m, 3H).

Example 399:

(6S)-6-methyl-3-[4-[methyl(oxazol-2-yl)carbamoyl]-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

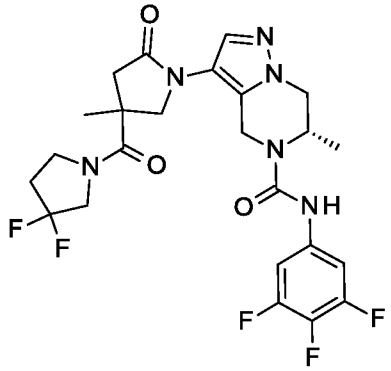


Preparation of (6S)-6-methyl-3-[4-[methyl(oxazol-2-yl)carbamoyl]-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 399):

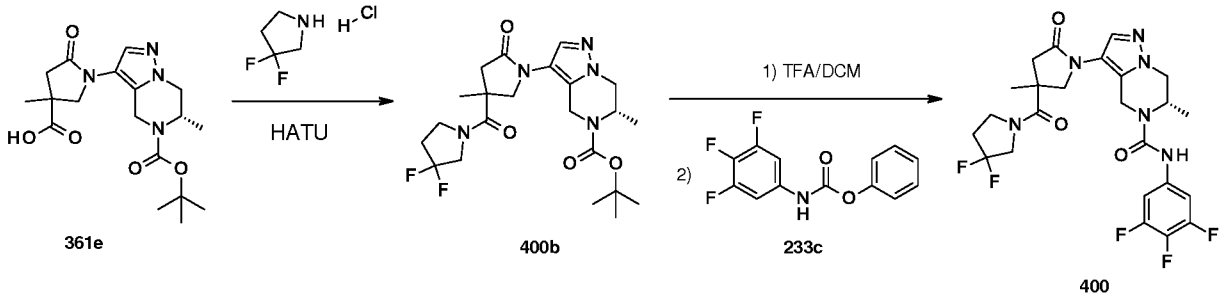
The title compound was prepared in analogy to **Example 384** by using N-methyl-2-Oxazolamine instead of 2-(methylamino)ethanol. **Example 399** was obtained as a white solid (13 mg). LCMS (M+H+): 518. ^{1}H NMR (400MHz, MeOD) δ ppm 7.87 (s, 1H), 7.63 (s, 1H), 7.34 - 7.25 (m, 2H), 7.20 (s, 1H), 5.07 - 4.93 (m, 2H), 4.54 - 4.46 (m, 1H), 4.33 - 4.26 (m, 1H), 4.18 - 3.98 (m, 4H), 3.41 (d, *J*=1.8 Hz, 3H), 2.88 - 2.77 (m, 2H), 1.31 - 1.25 (m, 3H).

Example 400:

(6S)-3-[4-(3,3-difluoropyrrolidine-1-carbonyl)-4-methyl-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: **preparation of (6S)-tert-butyl 3-(4-(3,3-difluoropyrrolidine-1-carbonyl)-4-methyl-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 400b)**

To a solution of 1-((S)-5-(tert-butoxycarbonyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)-3-methyl-5-oxopyrrolidine-3-carboxylic acid (compound **361e**, 120 mg, 317 μmol) in DCM (5 mL) was added 3,3-difluoropyrrolidine hydrochloride (68.3 mg, 476 μmol), DIPEA (377 mg, 0.5 mL, 2.92 mmol) and HATU (145 mg, 381 μmol). The reaction mixture was stirred at 40°C overnight and then was concentrated and purified by silica gel column to give compound **400b** (120 mg). LCMS ($M+H^+$): 468.

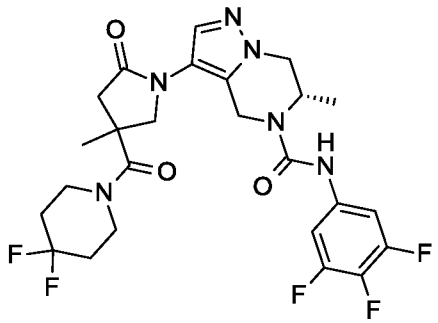
Step 2: preparation of (6S)-3-[4-(3,3-difluoropyrrolidine-1-carbonyl)-4-methyl-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 400)

A mixture of (6S)-tert-butyl 3-(4-(3,3-difluoropyrrolidine-1-carbonyl)-4-methyl-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **400b**, 120 mg, 257 μmol), trifluoroacetic acid (2.98 g, 2 mL, 26.1 mmol) and DCM (1 mL) was stirred at room temperature for 1 hour. The reaction mixture was concentrated. The residue was dissolved in DMF (2 mL), to which was added DIPEA (302 mg, 0.4 mL, 2.33 mmol), and phenyl (3,4,5-trifluorophenyl)carbamate (compound **233c**, 89.2 mg, 334 μmol). The reaction

mixture was stirred at 50 °C for 2 hours. Then the reaction mixture was concentrated and purified by prep-HPLC to give **Example 400** (56 mg). LCMS ($M+H^+$): 541. ^1H NMR (400MHz, CD_3OD) δ ppm 7.66 (m, 1H), 7.33 - 7.24 (m, 2H), 5.09-4.92 (m, 2H), 4.61 - 4.44 (m, 1H), 4.41 - 4.25 (m, 2H), 4.19-4.13 (m, 1H), 4.10 - 3.72 (m, 4H), 3.72-3.63 (m, 1H), 3.19 (br. s., 1H), 2.63-2.34 (m, 3H), 1.58 (br. s., 3H), 1.31-1.24 (m, 3H).

Example 401:

(6S)-3-[4-(4,4-difluoropiperidine-1-carbonyl)-4-methyl-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

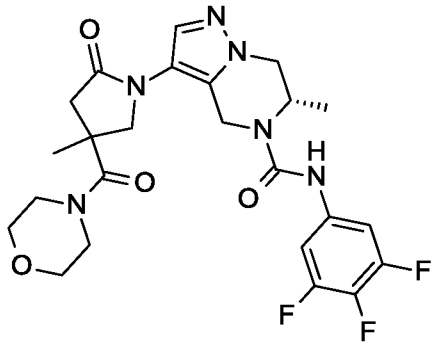


Preparation of (6S)-3-[4-(4,4-difluoropiperidine-1-carbonyl)-4-methyl-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 401):

The title compound was prepared in analogy to **Example 400** by using 4,4-difluoropiperidine hydrochloride instead of 3,3-difluoropyrrolidine hydrochloride. **Example 401** was obtained as a white solid (65 mg). LCMS (M+H+): 555. ^1H NMR (400MHz, MeOD) δ ppm 7.66 (s, 1H), 7.33-7.23 (m, 2H), 5.08 - 4.92 (m, 2H), 4.56 - 4.37 (m, 2H), 4.34-4.26 (m, 1H), 4.19-4.13 (m, 1H), 3.82 - 3.68 (m, 5H), 3.23 (dd, *J*=3.4, 16.9 Hz, 1H), 2.66 (dd, *J*=1.8, 17.1 Hz, 1H), 2.16 - 1.96 (m, 4H), 1.60 (s, 3H), 1.31-1.24 (m, 3H).

Example 402:

(6S)-6-methyl-3-[4-methyl-4-(morpholine-4-carbonyl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

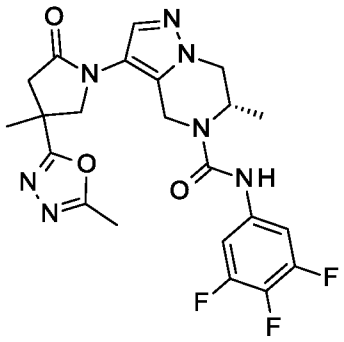


Preparation of (6S)-6-methyl-3-[4-methyl-4-(morpholine-4-carbonyl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 402):

The title compound was prepared in analogy to **Example 400** by using morpholine instead of 3,3-difluoropyrrolidine hydrochloride. **Example 402** was obtained as a white solid (54 mg). LCMS (M+H+): 521. ^{1}H NMR (400MHz, MeOD) δ ppm 7.66 (s, 1H), 7.32-7.24 (m, 2H), 5.03 (dd, *J*=13.6, 16.8 Hz, 2H), 4.57 - 4.36 (m, 2H), 4.33 - 4.26 (m, 1H), 4.21 - 4.12 (m, 1H), 3.77 - 3.58 (m, 9H), 3.26 - 3.17 (m, 1H), 2.66 (d, *J*=1.5 Hz, 1H), 1.59 (s, 3H), 1.32-1.24 (m, 3H).

Example 403:

(6S)-6-methyl-3-[4-methyl-4-(5-methyl-1,3,4-oxadiazol-2-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



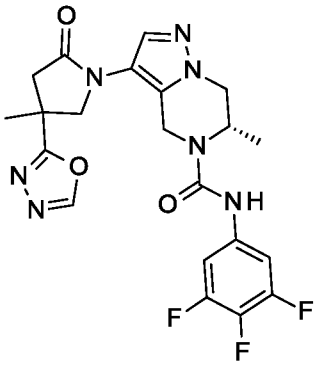
Preparation of (6S)-6-methyl-3-[4-methyl-4-(5-methyl-1,3,4-oxadiazol-2-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 403):

The title compound was prepared in analogy to **Example 283** by using (6S)-tert-butyl 3-(4-(methoxycarbonyl)-4-methyl-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **361d**) instead of (6S)-tert-butyl 3-(4-(methoxycarbonyl)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **236b**). **Example 403** was obtained as a white solid (64 mg). LCMS

(M+H+): 490. ^{1}H NMR (400MHz, MeOD) δ ppm 7.65 (s, 1H), 7.29 (ddd, *J*=3.1, 6.6, 10.1 Hz, 2H), 5.09 - 4.92 (m, 2H), 4.49 (dd, *J*=11.8, 17.1 Hz, 1H), 4.34 - 4.22 (m, 2H), 4.19 - 4.13 (m, 1H), 3.97 (dd, *J*=10.0, 14.3 Hz, 1H), 3.17 (d, *J*=17.1 Hz, 1H), 2.81 (d, *J*=17.1 Hz, 1H), 2.57 (d, *J*=2.8 Hz, 3H), 1.73 (s, 3H), 1.32 - 1.23 (m, 3H).

Example 404:

(6S)-6-methyl-3-[4-methyl-4-(1,3,4-oxadiazol-2-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

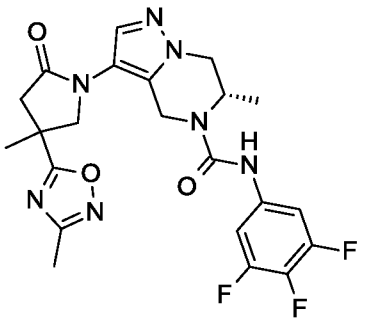


Preparation of (6S)-6-methyl-3-[4-methyl-4-(1,3,4-oxadiazol-2-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 404):

The title compound was prepared in analogy to **Example 282** by using (6S)-tert-butyl 3-(4-(methoxycarbonyl)-4-methyl-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **361d**) instead of (6S)-tert-butyl 3-(4-(methoxycarbonyl)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **236b**). **Example 404** was obtained as a white solid (12 mg). LCMS (M+H+): 476. 1H NMR (400MHz, MeOD) δ ppm 9.00 (s, 0.5H), 8.99 (s, 0.5H), 7.66 (s, 0.5H), 7.65 (s, 0.5H), 7.33 - 7.24 (m, 2H), 5.10 - 4.95 (m, 2H), 4.55-4.45 (m, 1H), 4.36 - 4.27 (m, 2H), 4.20 - 4.14 (m, 1H), 4.04-3.96 (m, 1H), 3.20 (d, *J*=17.1 Hz, 1H), 2.84 (d, *J*=16.8 Hz, 1H), 1.77 (s, 3H), 1.32-1.23 (m, 3H).

Example 405:

(6S)-6-methyl-3-[4-methyl-4-(3-methyl-1,2,4-oxadiazol-5-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

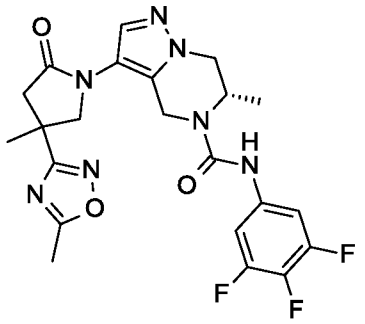


Preparation of (6S)-6-methyl-3-[4-methyl-4-(3-methyl-1,2,4-oxadiazol-5-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 405):

The title compound was prepared in analogy to **Example 284** by using 1-((S)-5-(tert-butoxycarbonyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)-3-methyl-5-oxopyrrolidine-3-carboxylic acid (compound **361e**) instead of 1-((S)-5-(tert-butoxycarbonyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)-5-oxopyrrolidine-3-carboxylic acid (compound **229a**). **Example 405** was obtained as a white solid (35 mg). LCMS (M+H+): 490. ^{1}H NMR (400MHz, MeOD) δ ppm 7.64 (s, 1H), 7.33-7.23 (m, 2H), 5.09 - 4.93 (m, 2H), 4.54-4.45 (m, 1H), 4.35 - 4.21 (m, 2H), 4.20 - 4.13 (m, 1H), 3.98 (dd, *J*=10.1, 14.9 Hz, 1H), 3.17 (dd, *J*=3.4, 16.9 Hz, 1H), 2.83 (d, *J*=17.0 Hz, 1H), 2.39 (d, *J*=3.5 Hz, 3H), 1.75 (s, 3H), 1.32-1.23 (m, 3H).

Example 406:

(6S)-6-methyl-3-[4-methyl-4-(5-methyl-1,2,4-oxadiazol-3-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

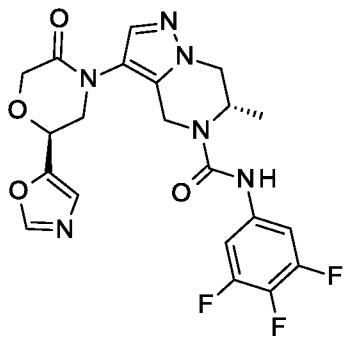


Preparation of (6S)-6-methyl-3-[4-methyl-4-(5-methyl-1,2,4-oxadiazol-3-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 406):

The title compound was prepared in analogy to **Example 285** by using (6S)-tert-butyl 3-(4-cyano-4-methyl-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **361g**) instead of (6S)-tert-butyl 3-(4-cyano-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **229c**). **Example 406** was obtained as a white solid (50 mg). LCMS (M+H+): 490. ^{1}H NMR (400MHz, MeOD) δ ppm 7.51 (s, 0.5H), 7.50 (s, 0.5H) 7.21 - 7.11 (m, 2H), 4.97 - 4.81 (m, 2H), 4.36 (dd, *J*=5.6, 17.0 Hz, 1H), 4.23 - 4.13 (m, 1H), 4.12 - 4.00 (m, 2H), 3.80 (dd, *J*=9.9, 14.8 Hz, 1H), 2.98 (dd, *J*=4.0, 16.9 Hz, 1H), 2.62 (d, *J*=16.9 Hz, 1H), 2.49 (d, *J*=3.7 Hz, 3H), 1.56 (s, 3H), 1.20-1.11 (m, 3H).

Example 407:

(6S)-6-methyl-3-[(2S)-2-oxazol-5-yl-5-oxo-morpholin-4-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

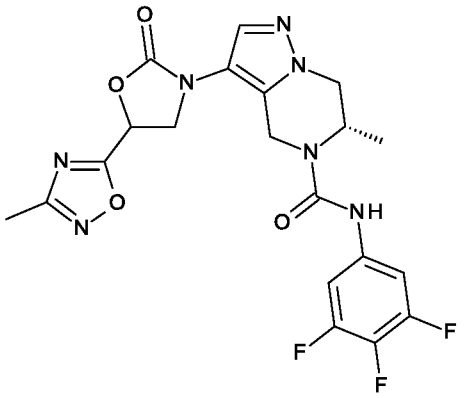


Preparation of (6S)-6-methyl-3-[(2S)-2-oxazol-5-yl-5-oxo-morpholin-4-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 407):

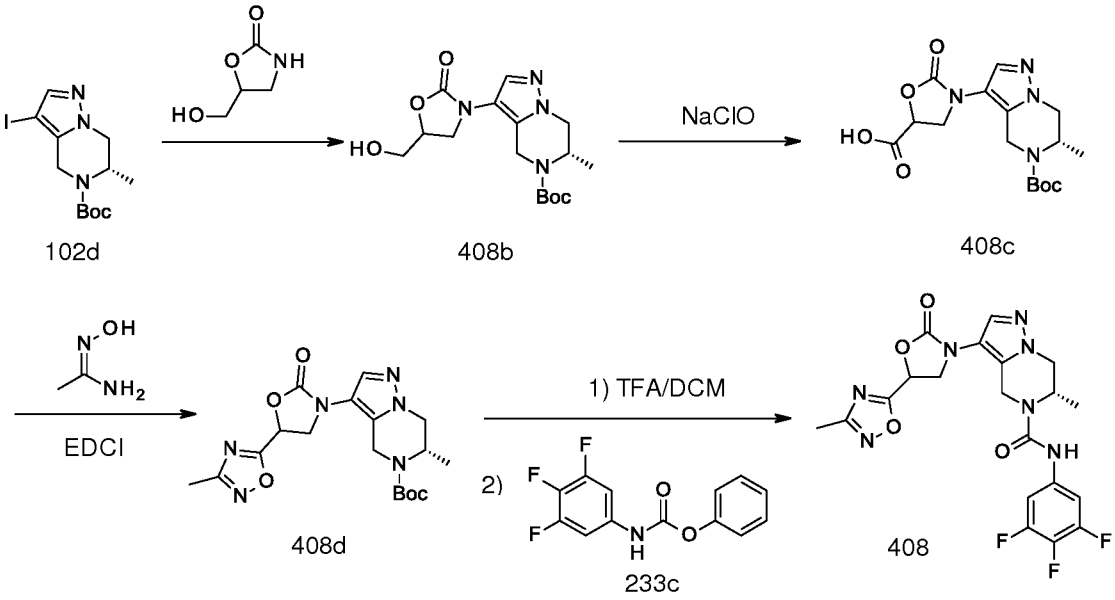
The title compound was prepared in analogy to **Example 247** by using (S)-6-(hydroxymethyl)morpholin-3-one instead of 4-(hydroxymethyl)pyrrolidin-2-one. **Example 407** was obtained as a white solid (4 mg). LCMS (M+H+): 477. ^{1}H NMR (400MHz, MeOD) δ ppm 8.28 (s, 1H), 7.70 (s, 1H), 7.33 - 7.24 (m, 3H), 5.34 (dd, *J*=3.4, 9.7 Hz, 1H), 5.03 - 4.92 (m, 2H), 4.56 - 4.40 (m, 3H), 4.35 - 4.14 (m, 3H), 3.95 (dd, *J*=3.4, 12.2 Hz, 1H), 1.29 (d, *J*=6.8 Hz, 3H).

Example 408:

(6S)-6-methyl-3-[5-(3-methyl-1,2,4-oxadiazol-5-yl)-2-oxo-oxazolidin-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: **preparation of (6S)-tert-butyl 3-(5-(hydroxymethyl)-2-oxooxazolidin-3-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 408b)**

A mixture of 5-(hydroxymethyl)oxazolidin-2-one (266 mg, 2.27 mmol), (6S)-tert-butyl 3-iodo-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **102d**,550 mg, 1.51 mmol), K_3PO_4 (643 mg, 3.03 mmol), CuI (57.7 mg, 303 μmol) and (1R,2R)-N1,N2-dimethylcyclohexane-1,2-diamine (43.1 mg, 303 μmol) in DMSO (15 mL) was stirred at 105 °C in microwave for 2 hours. After cooled down to room temperature, the reaction mixture was diluted with EtOAc, and washed with water. The aqueous phase was extracted with EtOAc three times. The combined organic layer was dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by silica gel column to give compound **408b** (300 mg). LCMS ($M+H^+$): 353.

Step 2: **preparation of 3-((S)-5-(tert-butoxycarbonyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)-2-oxooxazolidine-5-carboxylic acid (compound 408c)**

To a solution of (6S)-tert-butyl 3-(5-(hydroxymethyl)-2-oxooxazolidin-3-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **408b**, 740 mg, 2.1 mmol) in MeCN (2.1 mL) and water (21 mL) was added TEMPO (32.8 mg, 210 μmol) and Br (25 mg, 210 μmol). The reaction mixture was stirred for 10 minutes, to which was added dropwise NaCl (>14.5 % Cl) (3.86 mL, 18.9 mmol) aqueous solution and then 2N sodium hydroxide aqueous solution till pH=8-10. The reaction mixture was stirred at room temperature for 2 hours, and quenched by ethanol. The solvent was removed, and the residue was acidified to pH=4-5, and extracted with DCM/i-PrOH=5/1 twice. The organic layers were combined and concentrated to give crude compound **408c** (500 mg). LCMS ($M+H^+$): 367.

Step 3: **preparation of (6S)-tert-butyl 6-methyl-3-(5-(3-methyl-1,2,4-oxadiazol-5-yl)-2-oxooxazolidin-3-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 408d)**

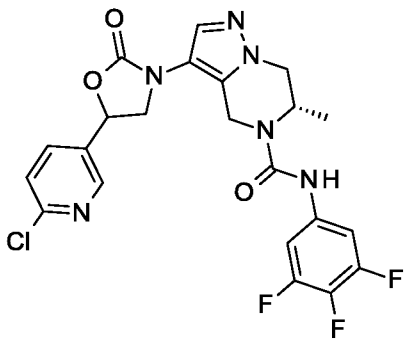
To a solution of N'-hydroxyacetimidamide (91 mg, 1.23 mmol) in DCM (8 mL) was added 3-((S)-5-(tert-butoxycarbonyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)-2-oxooxazolidine-5-carboxylic acid (compound **408c**, 150 mg, 409 μmol), N1-((ethylimino)methylene)-N3,N3-dimethylpropane-1,3-diamine hydrochloride (102 mg, 532 μmol), DIPEA (3.02 g, 4 mL, 23.3 mmol) and 1H-benzo[d][1,2,3]triazol-1-ol (16.6 mg, 123 μmol). The reaction mixture was sealed and stirred at 80 °C overnight. The reaction mixture was cooled down and concentrated. The residue was purified by silica gel column to give compound **408d** (66 mg). LCMS ($M+H^+$): 405.

Step 4: **preparation of (6S)-6-methyl-3-[5-(3-methyl-1,2,4-oxadiazol-5-yl)-2-oxo-oxazolidin-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 408)**

A mixture of (6S)-tert-butyl 6-methyl-3-(5-(3-methyl-1,2,4-oxadiazol-5-yl)-2-oxooxazolidin-3-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **408d**, 170 mg, 420 μmol), trifluoroacetic acid (2.98 g, 2 mL, 26.1 mmol) and DCM (1 mL) was stirred at room temperature for 1 hour. The reaction mixture was concentrated. The residue was dissolved in DMF (2 mL), to which was added DIPEA (754 mg, 1 mL, 5.83 mmol), and phenyl (3,4,5-trifluorophenyl)carbamate (compound **233c**, 146 mg, 546 μmol). The reaction mixture was stirred at 50°C for 2 hours, and then was purified by HPLC to give **Example 408** (27 mg). LCMS (M+H+): 478. ^{1}H NMR (400MHz, MeOD) δ ppm 7.70 (s, 1H), 7.32 - 7.24 (m, 2H), 6.03 (ddd, *J*=1.0, 5.1, 9.2 Hz, 1H), 5.11 (dd, *J*=11.2, 16.9 Hz, 1H), 5.02 - 4.92 (m, 1H), 4.61 - 4.45 (m, 2H), 4.40 - 4.28 (m, 2H), 4.22 - 4.14 (m, 1H), 2.45 (d, *J*=2.3 Hz, 3H), 1.31-1.24 (m, 3H).

Example 409:

(6S)-3-[5-(6-chloro-3-pyridyl)-2-oxo-oxazolidin-3-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

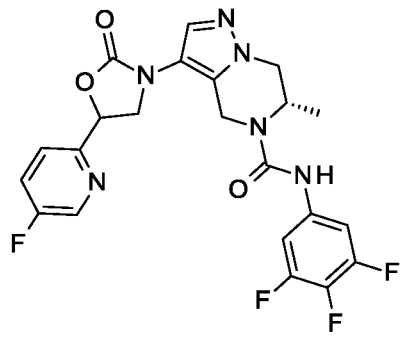


Preparation of (6S)-3-[5-(6-chloro-3-pyridyl)-2-oxo-oxazolidin-3-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 409):

The title compound was prepared in analogy to **Example 289** by using 6-chloropyridine-3-carbaldehyde instead of 1-methyl-1H-imidazole-2-carbaldehyde. **Example 409** was obtained as a white solid (66 mg). LCMS (M+H+): 507. ^{1}H NMR (400MHz, MeOD) δ ppm 8.54 (d, *J*=2.5 Hz, 1H), 8.06-8.11 (m, 1H), 7.69 (s, 0.5H), 7.69(s, 0.5H), 7.60 (d, *J*=8.5 Hz, 1H), 7.34 - 7.24 (m, 2H), 5.89 (t, *J*=8.3 Hz, 1H), 5.12 (dd, *J*=1.8, 16.8 Hz, 1H), 5.02 - 4.94 (m, 1H), 4.58 (d, *J*=16.8 Hz, 1H), 4.45 (td, *J*=9.0, 14.9 Hz, 1H), 4.35 - 4.27 (m, 1H), 4.21 - 4.14 (m, 1H), 4.03 (ddd, *J*=7.8, 9.0, 13.8 Hz, 1H), 1.30-1.25 (m, 3H).

Example 410:

(6S)-3-[5-(5-fluoro-2-pyridyl)-2-oxo-oxazolidin-3-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

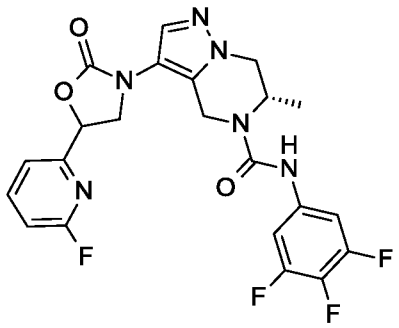


Preparation of (6S)-3-[5-(5-fluoro-2-pyridyl)-2-oxo-oxazolidin-3-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 410):

The title compound was prepared in analogy to **Example 289** by using 5-fluoropyridine-2-carbaldehyde instead of 1-methyl-1H-imidazole-2-carbaldehyde. **Example 410** was obtained as a white solid (65 mg). LCMS (M+H+): 491. ^{1}H NMR (400MHz, MeOD) δ ppm 8.59 (d, *J*=2.7 Hz, 1H), 7.77 - 7.65 (m, 3H), 7.33 - 7.24 (m, 2H), 5.85 (dd, *J*=6.5, 8.9 Hz, 1H), 5.18 - 5.09 (m, 1H), 5.01 - 4.93 (m, 1H), 4.56 (d, *J*=17.0 Hz, 1H), 4.44 (td, *J*=8.8, 14.1 Hz, 1H), 4.31 (dd, *J*=4.4, 12.7 Hz, 1H), 4.27 - 4.14 (m, 2H), 1.30-1.24 (m, 3H).

Example 411:

(6S)-3-[5-(6-fluoro-2-pyridyl)-2-oxo-oxazolidin-3-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

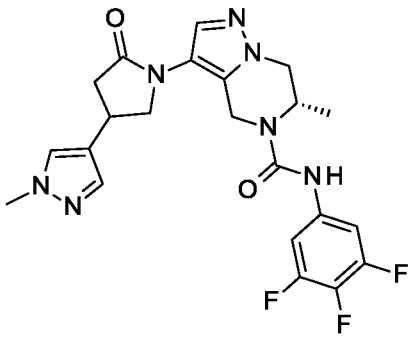


Preparation of (6S)-3-[5-(6-fluoro-2-pyridyl)-2-oxo-oxazolidin-3-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 411):

The title compound was prepared in analogy to **Example 289** by using 6-fluoropyridine-2-carbaldehyde instead of 1-methyl-1H-imidazole-2-carbaldehyde. **Example 411** was obtained as a white solid (84 mg). LCMS (M+H+): 491. ^{1}H NMR (400MHz, MeOD) δ ppm 8.06 (q, *J*=7.9 Hz, 1H), 7.68 (s, 0.5H), 7.67 (s, 0.5H), 7.53 (dd, *J*=2.1, 7.3 Hz, 1H), 7.33-7.23 (m, 2H), 7.12 (dd, *J*=2.2, 8.3 Hz, 1H), 5.87 - 5.74 (m, 1H), 5.16-5.06 (m, 1H), 5.03 - 4.92 (m, 1H), 4.62-4.53 (m, 1H), 4.49-4.39 (m, 1H), 4.30 (dd, *J*=4.4, 12.7 Hz, 1H), 4.21 - 4.08 (m, 2H), 1.31-1.23 (m, 3H).

Example 412:

(6S)-6-methyl-3-[4-(1-methylpyrazol-4-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

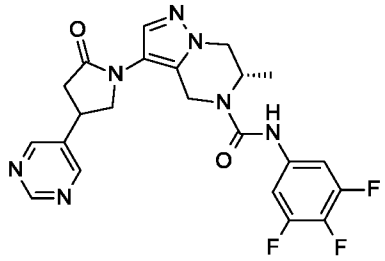


Preparation of (6S)-6-methyl-3-[4-(1-methylpyrazol-4-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 412):

The title compound was prepared in analogy to **Example 290** by using 1-methylpyrazole-4-carbaldehyde instead of thiazole-5-carbaldehyde. **Example 412** was obtained as a white solid (36 mg). LCMS (M+H+): 474. ^{1}H NMR (400MHz, MeOD) δ ppm 7.67 - 7.60 (m, 2H), 7.51 (s, 1H), 7.33-7.25 (m, 2H), 5.09-5.01 (m, 1H), 4.98 - 4.91 (m, 1H), 4.56-4.46 (m, 1H), 4.36 - 4.26 (m, 1H), 4.20 - 4.09 (m, 2H), 3.89 (s, 1.5H), 3.88 (s, 1.5H), 3.87 - 3.74 (m, 2H), 2.96-2.88 (m, 1H), 2.69-2.60 (m, 1H), 1.32-1.24 (m, 3H).

Example 413:

(6S)-6-methyl-3-(2-oxo-4-pyrimidin-5-yl-pyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

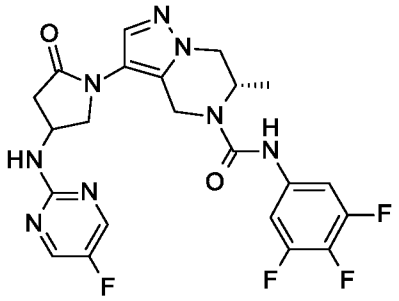


Preparation of (6S)-6-methyl-3-(2-oxo-4-pyrimidin-5-yl-pyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 413)

The title compound was prepared in analogy to Example **290** by using pyrimidine-5-carbaldehyde instead of thiazole-5-carbaldehyde. Example **413** (125 mg) was obtained as a white solid. LCMS (M+H$^+$): 472. ^{1}H NMR (400MHz, METHANOL-d_4) δ ppm 9.12 (s, 1H), 8.90 (s, 2H), 7.68 (s, 1H), 7.31-7.27 (m, 2H), 5.13-5.05 (m, 1H), 4.96 (br, 1H), 4.59-4.51 (m, 1H), 4.36 - 4.13 (m, 3H), 4.07 - 3.87 (m, 2H), 3.07-3.00 (m, 1H), 2.92 - 2.78 (m, 1H), 1.31-1.27 (m, 3H)

Example 414:

(6S)-3-[4-[(5-fluoropyrimidin-2-yl)amino]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

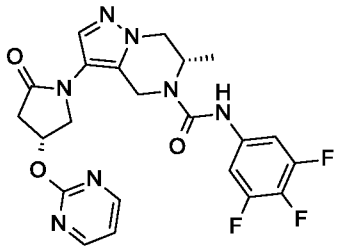


Preparation of (6S)-3-[4-[(5-fluoropyrimidin-2-yl)amino]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 414)

The title compound was prepared in analogy to Example **269** by using 2-bromo-5-fluoro-pyrimidine instead of 2-chloro-pyrimidine. Example **414** was obtained as a solid (20 mg). LCMS ($M+H^+$): 505. ^{1}H NMR (400MHz, METHANOL-d_4) δ ppm 8.30 (s, 2H), 7.63(s, 0.5H), 7.62(s, 0.5H), 7.30-7.26 (m, 2H), 5.08-5.03 (m, 1H), 4.98 - 4.91 (m, 1H), 4.75 - 4.64 (m, 1H), 4.57 - 4.44 (m, 1H), 4.35 - 4.19 (m, 2H), 4.15 (d, *J*=12.7 Hz, 1H), 3.76 (dt, *J*=4.2, 9.9 Hz, 1H), 3.01 (dd, *J*=8.3, 17.4 Hz, 1H), 2.61 (dd, *J*=4.9, 17.4 Hz, 1H), 1.29-1.26 (m, 3H)

Example 415:

(6S)-6-methyl-3-[(4R)-2-oxo-4-pyrimidin-2-yloxy-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



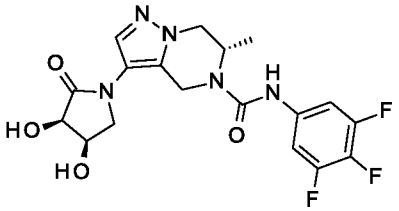
Preparation of Example 415

The title compound was prepared in analogy to Example **381** by using (R)-tert-butyl 3-((R)-4-hydroxy-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **376b**) instead of (S)-tert-butyl 3-((S)-4-hydroxy-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **377b**). Example

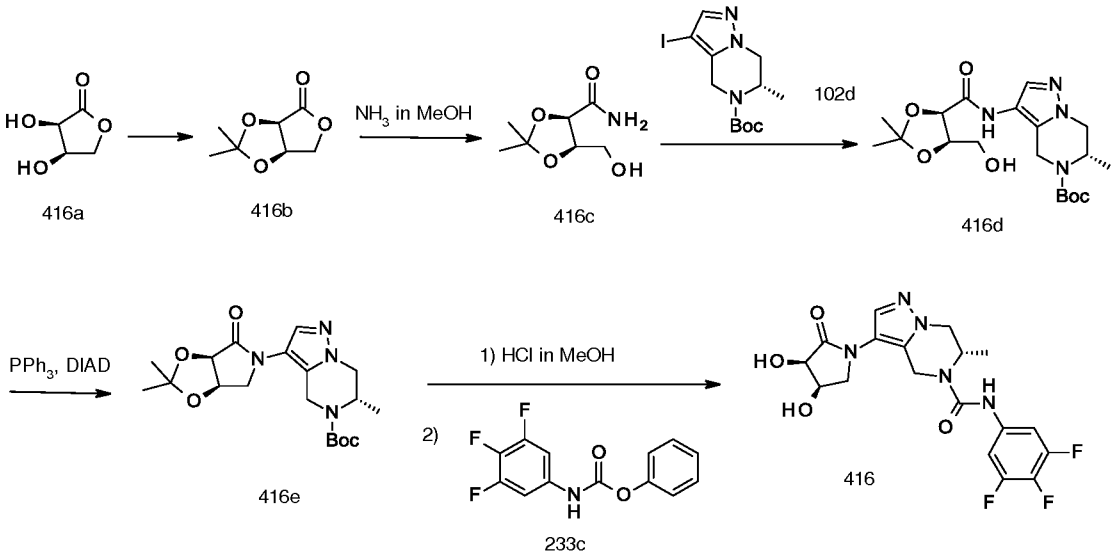
415 was obtained as a white solid (36 mg). LCMS ($M+H^+$): 488. ^1H NMR (400MHz, CD3OD) δ ppm 8.63 (d, *J*=4.9 Hz, 2H), 7.65 (s, 1H), 7.35 - 7.25 (m, 2H), 7.18 (t, *J*=4.8 Hz, 1H), 5.82-5.75 (m, 1H), 5.07 - 4.94 (m, 2H), 4.58 (d, *J*=16.9 Hz, 1H), 4.43 (dd, *J*=5.5, 11.5 Hz, 1H), 4.29 (dd, *J*=4.5, 12.8 Hz, 1H), 4.20 - 4.13 (m, 1H), 3.94 (dd, *J*=1.2, 11.5 Hz, 1H), 3.18 (dd, *J*=6.8, 18.1 Hz, 1H), 2.75 (dd, *J*=1.7, 18.1 Hz, 1H), 1.29 (d, *J*=7.0 Hz, 3H).

Example 416:

(6S)-3-[(3R,4R)-3,4-dihydroxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: Preparation of (3aR,6aR)-2,2-dimethyl-6,6a-dihydro-3aH-furo[3,4-d][1,3]dioxol-4-one (compound 416b)

A mixture of (3R,4R)-3,4-dihydroxydihydrofuran-2(3H)-one (2.36 g, 20 mmol), 2,2-dimethoxypropane (compound **416a**, 6.24 g, 60 mmol) and 4-methylbenzenesulfonic acid hydrate (380 mg, 2 mmol) in acetone (50 mL) was stirred at room temperature for 6 hours. The reaction mixture was then concentrated in *vacuo*, and the residue was purified by flash chromatography (silica gel, 40 g, 0% to 30% EtOAc in hexanes) to give compound **416b** as a light yellow solid (2.4 g).

Step 2: Preparation of (4R,5R)-5-(hydroxymethyl)-2,2-dimethyl-1,3-dioxolane-4-carboxamide (compound 416c)

A mixture of (3aR,6aR)-2,2-dimethyl-6,6a-dihydro-3aH-furo[3,4-d][1,3]dioxol-4-one (compound **416b**, 2.4 g, 15.2 mmol) and ammonia in methanol (7M, 21.7 mL, 152 mmol) was stirred at room temperature for 30 mins. The reaction mixture was concentrated in *vacuo* to give crude compound **416c** as a white solid (2.66 g). LCMS ($M+H^+$): 176.

Step 3: Preparation of (S)-tert-butyl 3-((4R,5R)-5-(hydroxymethyl)-2,2-dimethyl-1,3-dioxolane-4-carboxamido)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 416d)

A mixture of (4R,5R)-5-(hydroxymethyl)-2,2-dimethyl-1,3-dioxolane-4-carboxamide (compound **416c**, 724 mg, 4.13 mmol), (S)-tert-butyl 3-iodo-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **102d**, 1 g, 2.75 mmol), potassium phosphate (1.17 g, 5.51 mmol), copper(I) iodide (210 mg, 1.1 mmol) and (1R,2R)-N1,N2-dimethylcyclohexane-1,2-diamine (157 mg, 1.1 mmol) in DMSO (15 mL) was flushed with N_2 and sealed. The reaction mixture was heated in microwave at 120 °C for 2 hours, then diluted with water, extracted with DCM/i-PrOH (v/v=5/1). The combined organic layer was dried over Na_2SO_4 and then concentrated. The crude material was purified by flash chromatography (silica gel, 12 g, 10% to 30% MeOH in DCM) to give compound **416d** as light yellow oil (500 mg). LCMS ($M+H^+$): 411

Step 4: Preparation of (S)-tert-butyl 3-((3aR,6aR)-2,2-dimethyl-4-oxodihydro-3aH-[1,3]dioxolo[4,5-c]pyrrol-5(4H)-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 416e)

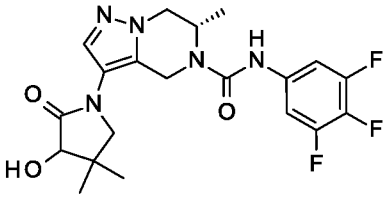
To a mixture of (S)-tert-butyl 3-((4R,5R)-5-(hydroxymethyl)-2,2-dimethyl-1,3-dioxolane-4-carboxamido)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **416d**, 500 mg, 1.22 mmol) and triphenylphosphine (383 mg, 1.46 mmol) in dry THF (10 mL) was added diisopropyl diazene-1,2-dicarboxylate (369 mg, 1.83 mmol) slowly at room temperature. The reaction mixture was stirred for 30 mins, and then concentrated in *vacuo*. The residue was purified by flash chromatography (silica gel, 12 g, 10% to 60% EtOAc in hexanes, where EtOAc contains 10% Methanol) to give compound **416e** as a light yellow oil (400mg). LCMS ($M+H^+$): 393.

Step 5: Preparation of (6S)-3-[(3R,4R)-3,4-dihydroxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 416)

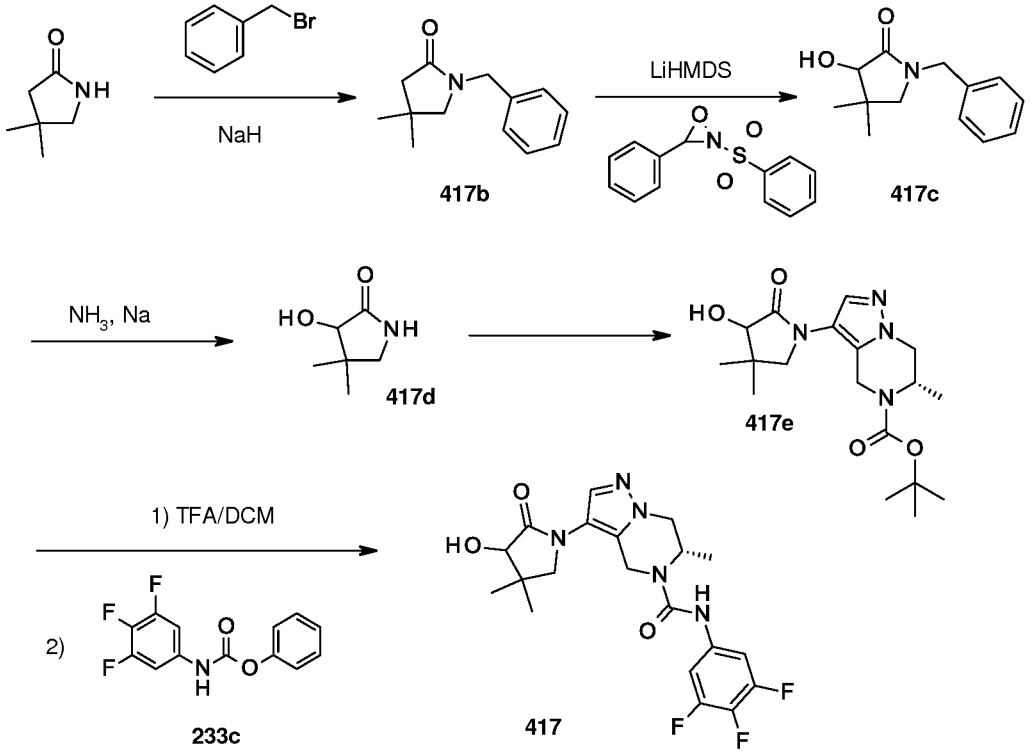
A mixture of (S)-tert-butyl 3-((3aR,6aR)-2,2-dimethyl-4-oxodihydro-3aH-[1,3]dioxolo[4,5-c]pyrrol-5(4H)-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **416e**, 50 mg, 127 μmol) in HCl/MeOH (5 mL) was stirred at room temperature for 12 hours, and then concentrated. The resulting residue was disolved in DMF (5 mL), to which was added N-ethyl-N-isopropylpropan-2-amine (82.3 mg, 637 μmol) and phenyl (3,4,5-trifluorophenyl)carbamate (40.9 mg, 153 μmol). The reaction mixture was stirred at 70 °C for 0.5 hours and then purified by prep-HPLC to give **Example 416** as a white solid (20mg). LCMS ($M+H^+$): 426. ^1H NMR (400MHz, METHANOL-d_4) δ ppm 7.62 (s, 1H), 7.33-7.28 (m, 2H), 5.11 (d, *J*=16.9 Hz, 1H), 5.02 - 4.94 (m, 1H), 4.55 - 4.38 (m, 3H), 4.35 - 4.26 (m, 1H), 4.17 (dd, *J*=1.2, 12.8 Hz, 1H), 4.03 (dd, *J*=3.7, 10.9 Hz, 1H), 3.59 (d, *J*=10.9 Hz, 1H), 1.25 (d, *J*=6.8 Hz, 3H)

Example 417:

(6S)-3-(3-hydroxy-4,4-dimethyl-2-oxo-pyrrolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: **preparation of 1-benzyl-4,4-dimethyl-pyrrolidin-2-one (compound 417b)**

To a solution of 4,4-dimethylpyrrolidin-2-one (1.5 g, 13.4 mmol) in DMF (20.0 mL) was added NaH (0.8 g, 20.0 mmol, 60%wt) at 0 °C. The reaction mixture was stirred at 0 °C for 1 hour, then to which was added bromomethylbenzene (2.3 g, 13.4 mmol). The resulting mixture was stirred at room temperature for another 16 hours, and then concentrated. The residue was purified by silica gel chromatography (PE/EtOAc= 3/1) to give compound **417b** as a colorless oil (2.3 g). LCMS ($M+H^+$): 204.

Step 2: preparation of 1-benzyl-3-hydroxy-4,4-dimethyl-pyrrolidin-2-one (compound 417c)

To a solution of 1-benzyl-4,4-dimethyl-pyrrolidin-2-one (compound **417b**, 2.7 g, 13.2 mmol) in THF (50.0 mL) was added a solution of LiHMDS in THF (26.6 mL, 26.6mmol) at -78 °C, and the reaction mixture was stirred at -78 °C for 1 hour, to which was then added a solution of 2-(benzenesulfonyl)-3-phenyl-oxaziridine (4.1 g, 15.8 mmol) in THF (10 mL), then the resulting mixture was allowed to warm slowly to room temperature, and stirred for additional 16 hours. The reaction mixture was concentrated and purified by prep-HPLC to give compound **417c** (1.3 g) as white solid. LCMS ($M+H^+$): 220.

Step 3: preparation of 3-hydroxy-4,4-dimethylpyrrolidin-2-one (compound 417d)

To a solution of 1-benzyl-3-hydroxy-4,4-dimethyl-pyrrolidin-2-one (compound **417c**, 1.0 g, 4.6 mmol) in THF (10.0 mL) at -78 °C was bubbled ammonia (~3 mL), followed by addition

of Na (1.05 g, 45.6 mmol). The reaction mixture was stirred at -78 °C for 10 mins, and then quenched with saturated aqueous solution of NH_4Cl (5.0 mL) and concentrated. The residue was taken up in PE/EA=1/1, and the solid was filtered off. The filtrate was concentrated to give crude compound **417d** (0.5g) as a white solid. LCMS ($M+H^+$): 130.

Step 4: preparation of (6S)-tert-butyl 3-(3-hydroxy-4,4-dimethyl-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 417e)

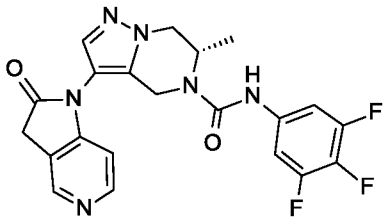
The reaction mixture of 3-hydroxy-4,4-dimethylpyrrolidin-2-one (53.3 mg, 413 μmol) , tert-butyl (6S)-3-iodo-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **102d**, 150 mg, 413 μmol), K_3PO_4 (175 mg, 826 μmol), CuI(15.7 mg, 82.6 μmol) and (1R,2R)-N1,N2-dimethylcyclohexane-1,2-diamine (11.7 mg, 82.6 μmol) in DMSO (7.0 mL) was flushed with nitrogen and sealed. The reaction mixture was stirred at 105 °C in microwave for 2 hours. After cooled down, the reaction mixture was diluted with ethyl acetate (30 mL), and washed with water. The aqueous phase was extracted with ethyl acetate three times. The combined organic layer was dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by silica gel column to give compound **417e** (100 mg). LCMS ($M+H^+$): 365.

Step 5: preparation of (6S)-3-(3-hydroxy-4,4-dimethyl-2-oxo-pyrrolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 417)

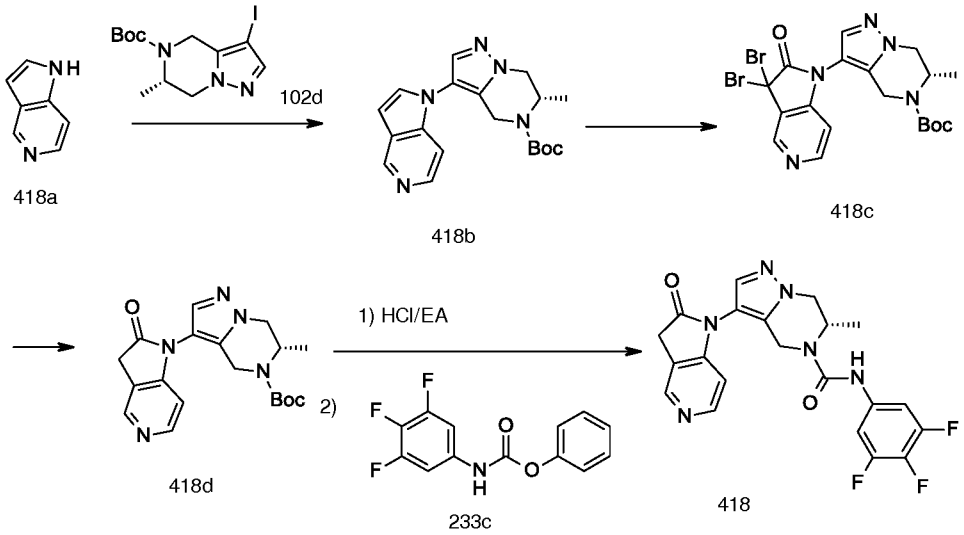
The reaction mixture of (6S)-tert-butyl 3-(3-hydroxy-4,4-dimethyl-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **417e**, 100 mg, 274 μmol) , TFA (2 mL) in DCM (1 mL) was stirred at room temperature for 1 hour. The reaction mixture was concentrated. The residue was dissolved in DCE (2.0 m:) , to which was then added DIPEA (742 mg, 1 mL, 5.74 mmol), and phenyl (3,4,5-trifluorophenyl)carbamate (95.3 mg, 357 μmol). The reaction mixture was stirred at 50°C for 2 hours. The reaction was concentrated and purified by prep-HPLC to give **Example 417** (60 mg). LCMS ($M+H^+$): 501. ^1H NMR (400MHz, CD_3OD) δ ppm 7.62 (s, 1H), 7.34 - 7.24 (m, 2H), 5.15 - 4.94 (m, 2H), 4.62 - 4.44 (m, 1H), 4.30 (dd, *J*=4.4, 12.7 Hz, 1H), 4.16 (d, *J*=13.8 Hz, 1H), 4.13 (d, *J*=5.0 Hz, 1H), 3.64 - 3.59 (m, 1H), 3.45 - 3.38 (m, 1H), 1.31 - 1.23 (m, 6H), 1.14 (s, 3H).

Example 418:

(6S)-6-methyl-3-(2-oxo-3H-pyrrolo[3,2-c]pyridin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: Preparation of tert-butyl (6S)-6-methyl-3-pyrrolo[3,2-c]pyridin-1-yl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 418b)

A mixture of 1H-pyrrolo[3,2-c]pyridine (compound **418a**, 500 mg, 4.3 mmol), (S)-tert-butyl 3-iodo-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **102d**, 1.72 g, 4.7 mmol), potassium phosphate (2.75 g, 13 mmol), copper(I) iodide (95 mg, 0.5 mmol) and (1R,2R)-N1,N2-dimethylcyclohexane-1,2-diamine (71 mg, 0.5 mmol) in dioxane (30 mL) was flushed with nitrogen. The reaction mixture was stirred at 120 °C for 12 hours and then concentrated. The residue was purified by prep-HPLC to give compound **418b** (600 mg) as a yellow oil. LCMS ($M+H^+$): 354.

Step 2: Preparation of tert-butyl (6S)-3-(3,3-dibromo-2-oxo-pyrrolo[3,2-c]pyridin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 418c)

To a solution of tert-butyl (6S)-6-methyl-3-pyrrolo[3,2-c]pyridin-1-yl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **418b**, 0.3 g, 0.85 mmol) in t-BuOH (4.0 mL) and H_2O (5.0 mL) was added a solution of Br_2 (0.5 g, 3.4 mmol) in t-BuOH (1.0 mL) dropwise at room temperature, then the reaction mixture was stirred at same temperature for 1 hour. The reaction mixture was basified to PH 6.5-7 with sodium bicarbonate solution, and extracted with EtOAc (20 mL). The organic phase was dried over Na_2SO_4 and concentrated to give compound **418c** as a yellow oil (0.4 g, crude).

Step 3: Preparation of tert-butyl (6S)-6-methyl-3-(2-oxo-3H-pyrrolo[3,2-c]pyridin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 418d)

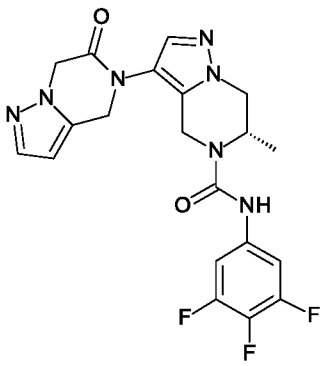
To a solution of tert-butyl (6S)-3-(3,3-dibromo-2-oxo-pyrrolo[3,2-c]pyridin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **418c**, 400.0 mg, 0.76 mmol) in EtOH (10.0 mL) was added Pd/C (40.0 mg), and the reaction mixture was stirred at room temperature for 12 hours under H_2 (50 psi) and then concentrated, the residue was purified by prep-HPLC to give compound **418d** (30.0 mg) as a brown oil. LCMS ($M+H^+$): 370

Step 4: Preparation of (6S)-6-methyl-3-(2-oxo-3H-pyrrolo[3,2-c]pyridin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 418)

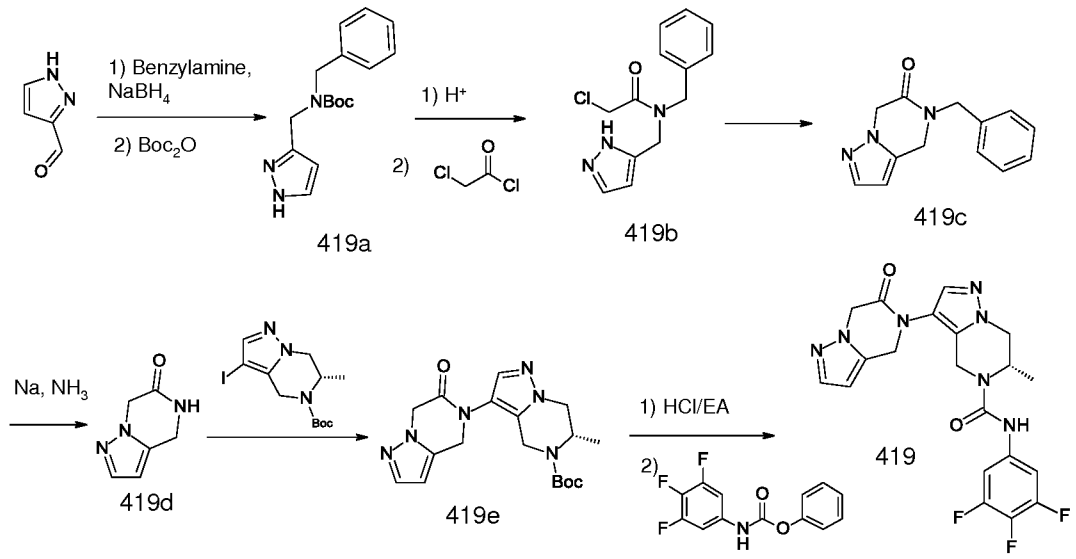
The title compound was prepared in analogy to Example **223** by using tert-butyl (6S)-6-methyl-3-(2-oxo-3H-pyrrolo[3,2-c]pyridin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **418d**) instead of tert-butyl (6S)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **223b**) and phenyl N-(3,4,5-trifluoro-phenyl)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). Example **413** was obtained as a white solid (6.0 mg). LCMS ($M+H^+$): 443.^{1}H NMR (400 MHz, DMSO-d6) δ ppm 9.05 (s, 1H), 8.45 - 8.37 (m, 2H), 7.74 (s, 1H), 7.42-7.37 (m, 2H), 6.82 (d, *J*=5.3 Hz, 1H), 4.97 - 4.86 (m, 2H), 4.41 - 4.15 (m, 3H), 3.83 (s, 2H), 1.18 (d, *J*=6.8 Hz, 3H).

Example 419:

(6S)-6-methyl-3-(6-oxo-4,7-dihydropyrazolo[1,5-a]pyrazin-5-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of tert-butyl N-benzyl-N-(1H-pyrazol-3-ylmethyl)carbamate (compound 419a)

To the solution of 1H-pyrazole-3-carbaldehyde (5.00 g, 52.03 mmol) in MeOH (50 mL) was added benzylamine (5.58 g, 52.03 mmol) at room temperature. After stirred at same temperature for 1 hour, the reaction mixture was cooled to 0 °C, and to which was added $NaBH_4$(1.97 g, 52.03 mmol) slowly. Ten minutes later, H_2O (10 mL) was added to the reaction mixture slowly at 0 °C, followed by $(Boc)_2O$ (11.36 g, 52.03 mmol). The resulting mixture was stirred at room temperature for 3 hours, and then most of the solvent was removed under vacuum. The residue was taken up in brine (100 mL), and extracted with EtOAc (100 mL) three times. The combined organic layer was dried over Na_2SO_4 and concentrated to give a crude product, which was purified by silica gel column chromatography (eluent: PE/EtOAc=7:1 to 3:1) to give compound **419a** as a colorless oil (10.5 g). LCMS ($M+H^+$): 288.2

Preparation of N-benzyl-2-chloro-N-(1H-pyrazol-5-ylmethyl)acetamide (compound 419b)

To a solution of tert-butyl N-benzyl-N-(1H-pyrazol-3-ylmethyl)carbamate (compound **419a**, 5.0 g, 17.4 mmol) in EtOAc(20 mL) was added EtOAc/HCl (1M, 50 mL) at 0 °C. The reaction mixture was stirred at room temperature for 2 hours, and then filtered. The filter cake was washed with EtOAc (30 mL), dried, and collected to give 1-phenyl-N-(1H-pyrazol-3-ylmethyl)methanamine in HCl salt form (3.90 g, crude) as a white solid. To a suspension of 1-phenyl-N-(1H-pyrazol-3-ylmethyl)methanamine hydrochloride (3.90 g, 17.4 mmol) in DCM (50 mL) at 0 °C was added TEA (5.28 g,52.2 mmol) and 2-chloroacetyl chloride (2.95 g, 26.1 mmol). The reaction mixture was stirred at room temperature for 2 hours and then poured into H_2O (100 mL). The aqueous phase was extracted with EtOAc (100 mL) three times, and the combined

organic layer was washed with brine (100 mL), and concentrated. The obtained residue was purified by silica gel column chromatography (PE/EtOAc=1/2-1/4) to give compound **419b** as a colorless oil (3.50 g). LCMS (M+1): 264.1

Preparation of 5-benzyl-4,7-dihydropyrazolo[1,5-a]pyrazin-6-one (compound 419c)

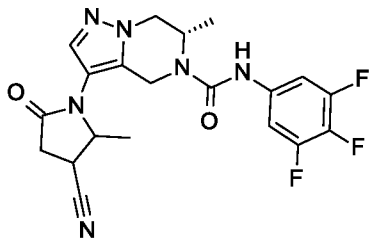
To a suspension of NaH (0.92 g, 22.75 mmol) in THF (50 mL) at 70 °C under nitrogen was added dropwise a solution of N-benzyl-2-chloro-N-(1H-pyrazol-5-ylmethyl)acetamide (3.0 g, 11.37 mmol) in THF (50 mL). After completion of addition, the reaction mixture was stirred at 70 °C for 1 hour, and then cooled to room temperature. The reaction mixture was poured into saturated NH_4Cl aqueous solution (50 mL) and extracted with EtOAc (50 mL) three times. The combined organic layer was dried over Na_2SO_4 and concentrated. The obtained residue was purified by silica gel column chromatography (PE/EtOAc=1/2-1/3) to give compound **419c** as a white solid (700 mg). LCMS (M+1): 228.1

Preparation of (6S)-6-methyl-3-(6-oxo-4,7-dihydropyrazolo[1,5-a]pyrazin-5-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (example 419)

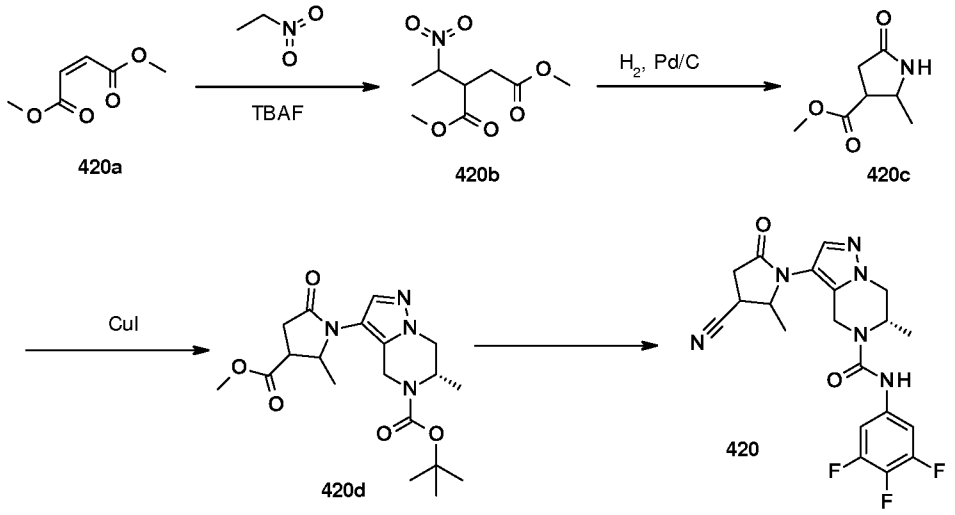
The title compound was prepared in analogy to **Example 417** by using 5-benzyl-4,7-dihydropyrazolo[1,5-a]pyrazin-6-one (compound **419c**) instead of 1-benzyl-3-hydroxy-4,4-dimethyl-pyrrolidin-2-one (compound **417c**). **Example 417** was obtained as a white solid (6.4 mg). LCMS (M+1): 446.2; ^{1}H NMR (300 MHz, DMSO-d^6) ppm 9.01 (s, 1H), 7.68 (s, 1H), 7.56 (s, 1H), 7.50-7.25 (m, 2H), 6.24 (s, 1H), 5.15 - 4.80 (m, 6H), 4.39 - 4.03 (m, 3H), 1.14 (d, J=6.2 Hz, 3H)

Example 420:

(6S)-3-(3-cyano-2-methyl-5-oxo-pyrrolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of dimethyl 2-(1-nitroethyl)butanedioate (compound 420b)

To a mixture of dimethyl (Z)-but-2-enedioate (compound **420a**, 10.0 g, 69.4 mmol) and nitroethane (60 mL) in THF (500 mL) was added a solution of tetrabutylammonium fluoride (7.0 mmol) in THF (7 mL). The reaction mixture was stirred at room temperature for 2 hours, and then quenched with saturated NH_4Cl aqueous solution. The aqueous phase was extracted with DCM three times. The combined organic layer was dried over Na_2SO_4, filtrated and concentrated. The residue was purified by silica gel column to give compound **420b** as a yellow oil (10 g). LCMS ($M+H^+$): 220.

Preparation of methyl 2-methyl-5-oxo-pyrrolidine-3-carboxylate (compound 420c)

To a solution of dimethyl 2-(1-nitroethyl)butanedioate (compound **420b**, 8.0 g, 36.4 mmol) in EtOH (100 mL) was added Pd/C (400 mg). The reaction mixture was stirred under 1 atm of H_2 at 50 °C for 24 hours, and then concentrated. The residue was purified by prep-HPLC to give compound **420c** as a light-red oil (3.6 g). LCMS ($M+H^+$): 158.

Preparation of tert-butyl (6S)-3-(3-methoxycarbonyl-2-methyl-5-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 420d)

To a solution of tert-butyl (6S)-3-iodo-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **102d**,3.8 g, 10.5 mmol) in dioxane (50 mL) was added methyl 2-methyl-5-oxo-pyrrolidine-3-carboxylate (compound **420c**, 1.5 g, 9.5 mmol), (1R,2R)-N1,N2-dimethylcyclohexane-1,2-diamine (142.2 mg, 1.0 mmol), K_3PO_4 (6.1 g, 28.5 mmol), and CuI (190.5 mg, 1.0 mmol) under nitrogen at 25 °C. The reaction mixture was stirred at 120 °C for 16 hours. After cooled down to room temperature, the reaction mixture was filtered, and concentrated. The resulting residue was purified by silica gel column and prep-HPLC (TFA)

sequentially to give compound **420d** (2.0 g) as white solid. LCMS (M+1): 393. Compound **420d** was then subjected to chiral SFC separation to give four isomers.

Compound **420d-1** (93.4 mg). ^{1}H NMR (400MHz, DMSO-d^6) δ ppm 7.47 (s, 1H), 4.78 (d, *J*=17.2 Hz, 1H), 4.65 (br. s., 1H), 4.22 - 4.00 (m, 4H), 3.69 (s, 3H), 3.09 - 3.00 (m, 1H), 2.73 (dd, *J*=16.8, 9.2 Hz, 1H), 2.60 (dd, *J*=16.8, 7.2 Hz, 1H), 1.43 (s, 9H), 1.20 (d, *J*=6.3 Hz, 3H), 1.01 (d, *J*=6.8 Hz, 3H).

Compound **420d-2** (230.3 mg). ^{1}H NMR (400MHz, DMSO-d^6) δ ppm 7.50 (s, 1H), 4.66 (brs., 1H), 4.57 (d, *J*=17.4 Hz, 1H), 4.35 - 4.25 (m, 1H), 4.18 (d, *J*=17.2 Hz, 1H), 4.17-4.10 (m, 1H), 4.03 (d, *J*=12.8 Hz, 1H), 3.68 (s, 3H), 3.60 (q, *J*=8.1 Hz, 1H), 2.70 (dd, *J*=16.8, 8.0 Hz, 1H), 2.55-2.45 (m, 1H), 1.43 (s, 9H), 1.09 (d, *J*=6.9 Hz, 3H), 0.97 (d, *J*=6.5 Hz, 3H).

Compound **420d-3** (245.5 mg). ^{1}H NMR (400MHz, DMSO-d$_6$) δ ppm 7.52 (s, 1H), 4.80 (d, *J*=17.4 Hz, 1H), 4.64 (brs., 1H), 4.38 - 4.24 (m, 1H), 4.23 - 4.11 (m, 1H), 4.08 - 3.95 (m, 2H), 3.68 (s, 3H), 3.61 (q, *J*=8.4 Hz, 1H), 2.71 (dd, *J*=16.8, 8.4 Hz, 1H), 2.56 - 2.52 (m, 1H), 1.44 (s, 9H), 1.00 (d, *J*=6.8 Hz, 3H), 0.95 (d, *J*=6.5 Hz, 3H).

Compound **420d-4** (97.9 mg). ^{1}H NMR (400MHz, DMSO-d$_6$) δ ppm 7.48 (s, 1H), 4.66 (brs., 1H), 4.59 (d, *J*=17.3 Hz, 1H), 4.23 - 3.99 (m, 4H), 3.69 (s, 3H), 3.13 - 3.01 (m, 1H), 2.76 (dd, J=17.2, 9.2 Hz, 1H), 2.60 (dd, J=17.0, 7.2 Hz, 1H), 1.43 (s, 9H), 1.20 (d, *J*=6.3 Hz, 3H), 1.08 (d, *J*=6.9 Hz, 3H).

Preparation of (6S)-3-(3-cyano-2-methyl-5-oxo-pyrrolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 420)

The title compound was prepared in analogy to Example **240** by using tert-butyl (6S)-3-(3-methoxycarbonyl-2-methyl-5-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **420d**) instead of (6S)-tert-butyl 3-(4-(methoxycarbonyl)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **236b**).

Example **420-1** was obtained as a white solid (17 mg). LCMS (M+H+): 433. ^{1}H NMR (400MHz, CD_3OD) δ ppm 7.46 (s, 1H), 7.21 - 7.12 (m, 2H), 4.88 (d, *J*=16.9 Hz, 1H), 4.85 - 4.80 (m, 1H), 4.25 - 4.17 (m, 3H), 4.06 (d, *J*=12.7 Hz, 1H), 3.27 - 3.23 (m, 1H), 2.88(dd, *J*=17.0, 9.0 Hz, 1H), 2.78(dd, *J*=17.0, 8.8 Hz, 1H), 1.25 (d, *J*=6.4 Hz, 3H), 1.10 (d, *J*=6.7 Hz, 3H).

Example **420-2** was obtained as a white solid (59 mg). LCMS (M+H+): 433. ^{1}H NMR (400MHz, CD_3OD) δ ppm 7.59 (s, 1H), 7.32 - 7.23 (m, 2H), 5.01 - 4.93 (m, 1H), 4.91 - 4.89 (m, 1H), 4.48 (d, *J*=16.9 Hz, 1H), 4.43 - 4.29 (m, 2H), 4.17 (d, *J*=12.4 Hz, 1H), 3.92 (td, *J*=9.0, 7.2

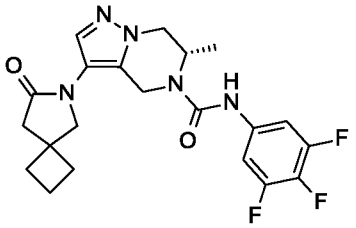
Hz, 1H), 2.99 (dd, *J*=17.0, 9.0 Hz, 1H), 2.90 (dd, *J*=17.0, 7.0 Hz, 1H), 1.41 (d, *J*=6.5 Hz, 3H), 1.29 (d, *J*=7.0 Hz, 3H).

Example **420-3** was obtained as a white solid (40 mg). LCMS (M+H+): 433. ^{1}H NMR (400MHz, CD_3OD) δ ppm 7.58 (s, 1H), 7.35 - 7.24 (m, 2H), 5.05 - 4.94 (m, 2H), 4.40 - 4.29 (m, 3H), 4.18 (d, *J*=12.8 Hz, 1H), 3.91 (td, *J*=8.9, 7.0 Hz, 1H), 3.00 (dd, *J*=17.0, 9.0 Hz, 1H), 2.90 (dd, *J*=17.0, 6.7 Hz, 1H), 1.42 (d, *J*=6.6 Hz, 3H), 1.23 (d, *J*=6.8 Hz, 3H).

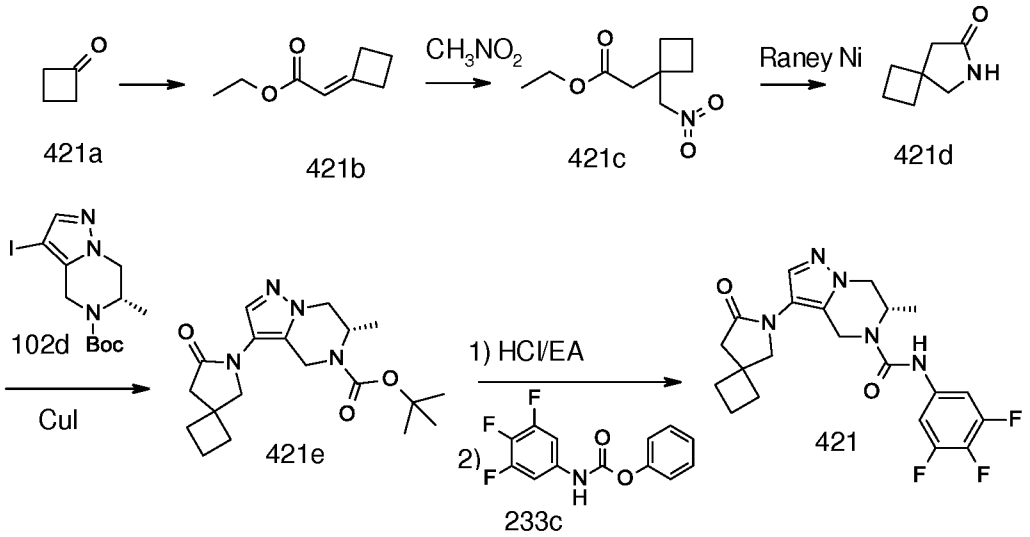
Example **420-4** was obtained as a white solid (54 mg). LCMS (M+H+): 433. ^{1}H NMR (400MHz, CD_3OD) δ ppm 7.59 (s, 1H), 7.31 - 7.23 (m, 2H), 5.00 - 4.92 (m, 1H), 4.92 - 4.84 (m, 1H), 4.46 (d, *J*=17.0 Hz, 1H), 4.40 - 4.28 (m, 2H), 4.17 (d, *J*=12.8 Hz, 1H), 3.37 - 3.34 (m, 1H), 3.00 (dd, *J*=17.0, 9.1 Hz, 1H), 2.89 (dd, *J*=17.0, 8.7 Hz, 1H), 1.36 (d, *J*=6.4 Hz, 3H), 1.30 (d, *J*=6.8 Hz, 3H).

Example 421:

(6S)-6-methyl-3-(7-oxo-6-azaspiro[3.4]octan-6-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of 6-azaspiro[3.4]octan-7-one (compound421d)

Step 1: To a solution of methyl 2-(dimethoxyphosphoryl) acetate (36.4 g, 199.7 mmol) in THF was added NaH (7.4 g, 185.4 mmol) with ice bath cooling. The resulting mixture was

stirred at the same temperature for 1 hour, and then a solution of cyclobutanone (compound **421a**, 10.0 g, 142.7 mmol) in THF (100 mL) was added. The mixture was then warmed to room temperature and stirred for 11 hours and quenched with saturated aqueous ammonium chloride (100 mL). The mixture was extracted with hexane (500 mL). The organic layer was washed with brine (200 mL) twice, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give compound **421b** as a pale yellow oil (18.9 g).

Step 2: To a solution of methyl 2-cyclobutylideneacetate (compound **421b**, 18.0 g, 142.7 mmol) in nitromethane (180 mL) was added DBU (21.7 g, 14.7 mmol). The mixture was stirred at 25 °C for 4 hours, and then concentrated under reduced pressure. The residue was purified by column chromatography to give compound **421c** as a pale yellow oil (21.1 g).

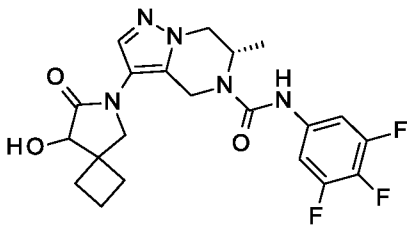
Step 3: To a solution of methyl 2-[1-(nitromethyl)cyclobutyl]acetate (compound **421c**, 10.0 g, 53.4 mmol) in MeOH (100 mL) was added Raney Ni (1.0 g). The mixture was stirred at 50 °C under 50 psi of hydrogen for 4 hours and then filtered. The filtrated was concentrated under reduced pressure to give compound **421d** as a white solid (5.9 g). LCMS ($M+H^+$): 126.

Preparation of (6S)-6-methyl-3-(7-oxo-6-azaspiro[3.4]octan-6-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 421)

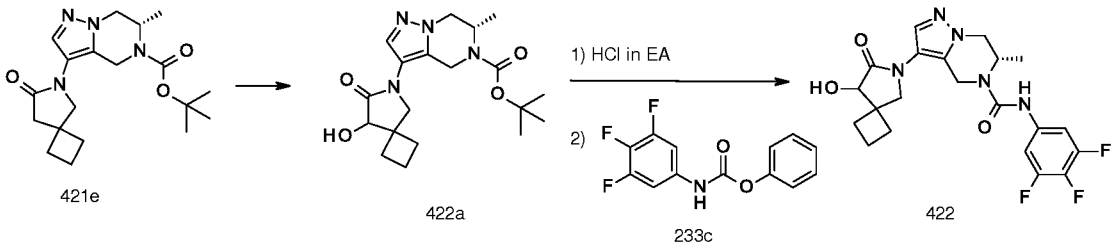
The title compound was prepared in analogy to **Example 223** by using 6-azaspiro[3.4]octan-7-one (compound **421d**) instead of pyrrolidin-2-one and phenyl N-(3,4,5-trifluorophenyl)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 421** was obtained as a white solid (8 mg). LCMS ($M+H^+$): 434. ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.98 (br. s., 1H), 7.30 (s, 1H), 7.17 (d, 2H), 5.12-4.91 (m, 2H), 4.34-4.13 (m, 2H), 3.92 (d, 1H), 3.82 (d, 1H), 3.67 (d, 1H), 2.62 (s, 2H), 2.23-2.01 (m, 4H), 2.00-1.83 (m, 2H), 1.30 (d, 3H).

Example 422:

(6S)-3-(8-hydroxy-7-oxo-6-azaspiro[3.4]octan-6-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



421e 422a 233c 422

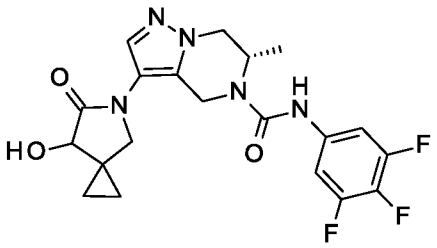
Preparation of tert-butyl (6S)-3-(8-hydroxy-7-oxo-6-azaspiro[3.4]octan-6-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 422a):

To a solution of tert-butyl (6S)-6-methyl-3-(7-oxo-6-azaspiro[3.4]octan-6-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **421e**, 190 mg, 0.53 mmol) in THF (5 mL) was added LiHMDS (1.1 mL, 1.1 mmol) at -78 °C. The mixture was stirred at -78 °C for 30 minutes, then 3-phenyl-2-(phenylsulfonyl)-1,2-oxaziridine (165 mg, 0.63 mmol) was added. The resulting mixture was allowed to warm to room temperature and stirred for 1.5 hours, and then quenched with H_2O (5 mL). The mixture was concentrated under reduced pressure, and the residue was purified by prep-HPLC to give compound **422a** as a yellow oil (90 mg). LCMS ($M+H^+$): 377.

Preparation of (6S)-3-(8-hydroxy-7-oxo-6-azaspiro[3.4]octan-6-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 422)

A mixture of tert-butyl (6S)-3-(8-hydroxy-7-oxo-6-azaspiro[3.4]octan-6-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **422a**, 90 mg, 0.24 mmol) in a solution of HCl in EtOAc (10 mL, 4 M) was stirred at 20 °C for 2 hours. Then the mixture was concentrated. To the residue was added triethylamine (73 mg, 0.72 mmol) and phenyl N-(3,4,5-trifluorophenyl)carbamate (**compound 233c**, 64 mg, 0.24 mmol) in DMF (4 mL). The mixture was stirred at 20 °C for 4 hours, and then concentrated under reduced pressure. The residue was purified by prep-HPLC to give **Example 422** as a white solid (10 mg). LCMS ($M+H^+$): 450. ^1H NMR (400 MHz, DMSO-d_6) δ ppm 7.56 (d, 1H), 7.48-7.32 (m, 2H), 5.07-4.97 (m, 1H), 4.94-4.83 (m, 1H), 4.47-4.34 (m, 1H), 4.27-4.17 (m, 1H), 4.13-3.95 (m, 2H), 3.82-3.72 (m, 1H), 3.70-3.60 (m, 1H), 2.22-1.68 (m, 6H), 1.24-1.10 (m, 3H).

Example 424:
(6S)-3-(7-hydroxy-6-oxo-5-azaspiro[2.4]heptan-5-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

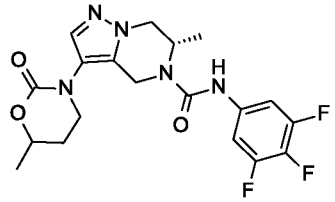


Preparation of (6S)-3-(7-hydroxy-6-oxo-5-azaspiro[2.4]heptan-5-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 424)

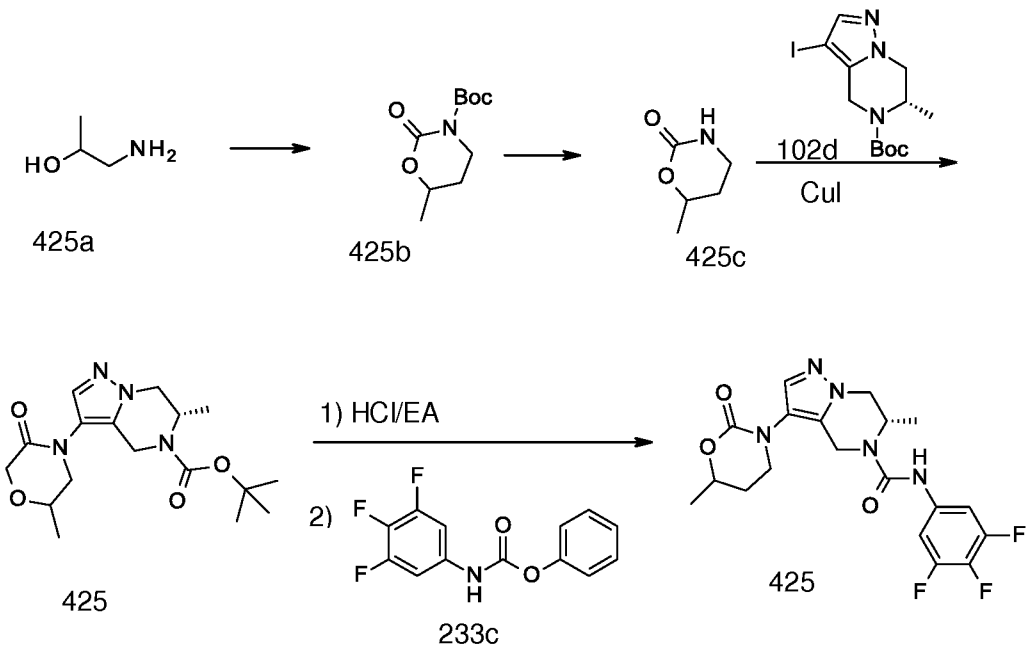
The title compound was prepared in analogy to **Example 422** by using tert-butyl (6S)-6-methyl-3-(6-oxo-5-azaspiro[2.4]heptan-5-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **252e**) instead of tert-butyl (6S)-6-methyl-3-(7-oxo-6-azaspiro[3.4]octan-6-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **421e**). **Example 424** was obtained as a white solid (124 mg). LCMS ($M+H^+$): 436. ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.87-7.41 (m, 2H), 7.26 - 7.16 (m, 2H), 5.26-4.98 (m, 2H), 4.55-4.25 (m, 3H), 4.12-3.46 (m, 3H), 3.37 (br. s., 1H), 1.34 (dd, 3H), 1.30-1.22 (m, 1H), 0.95-0.81 (m, 2H), 0.66-0.54 (m, 1H).

Example 425:

(6S)-6-methyl-3-(6-methyl-2-oxo-1,3-oxazinan-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of 6-methyl-1,3-oxazinan-2-one (compound 425c)

Step 1: A solution of Boc_2O (1.5 g, 6.73 mmol), triethylamine (682 mg, 6.73 mmol) and DMAP (55 mg, 0.45 mmol) in CH_3CN (5 mL) was stirred at 20 °C for 1 hour. To the above solution was added a solution of 4-aminobutan-2-ol (compound **425a**, 200 mg, 2.25 mmol) in CH_3CN (5 mL). The resulting mixture was stirred at 20 °C for 12 hours and then concentrated under reduced pressure. The residue was purified by prep-HPLC to give compound **425b** as a colorless oil (320 mg).

Step 2: To a solution of tert-butyl 6-methyl-2-oxo-1,3-oxazinane-3-carboxylate (compound **425b**, 200 mg, 0.93 mmol) in DCM (3 mL) was added TFA (0.3 mL). The mixture was stirred at 20 °C for 16 hours and then partitioned between DCM (50 mL) and saturated aqueous $NaHCO_3$ solution (20 mL). The organic layer was washed with brine (20 mL), dried over anhydrous Na_2SO_4 and concentrated to give compound **425c** as a yellow solid (60 mg). LCMS ($M+H^+$): 116.

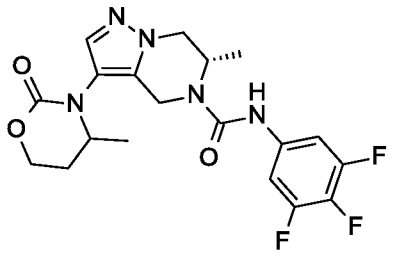
Preparation of (6S)-6-methyl-3-(6-methyl-2-oxo-1,3-oxazinan-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 425)

The title compound was prepared in analogy to **Example 223** by using 6-methyl-1,3-oxazinan-2-one (compound **425c**) instead of pyrrolidin-2-one and phenyl N-(3,4,5-trifluorophenyl)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 425** was obtained as a white solid (46 mg). LCMS ($M+H^+$): 424. ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.74-7.52 (m, 1H), 7.41 (d, 1H), 7.18-7.07 (m, 2H), 5.07-4.94 (m, 1H), 7.92-4.73 (m, 1H), 4.61-4.47 (m, 1H), 4.31-4.12 (m, 2H), 3.95 (dd, 1H), 3.89-3.70 (m, 1H), 3.66-3.46 (m, 1H), 2.18-2.05 (m, 1H), 2.04-1.89 (m, 1H), 1.43 (d,

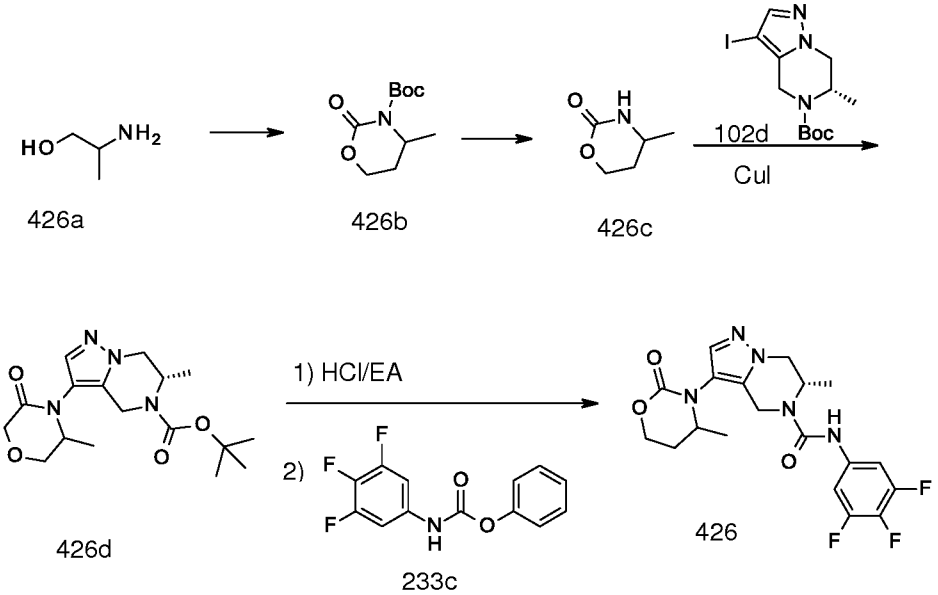
3H), 1.26 (t, 3H).

Example 426:

(6S)-6-methyl-3-(4-methyl-2-oxo-1,3-oxazinan-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of 4-methyl-1,3-oxazinan-2-one (compound 426c)

The compound **426c** was prepared in analogy to compound **425c** by using 3-aminobutan-1-ol (compound **426a**) instead of 4-aminobutan-2-ol (compound **425a**). Compound **426c** was obtained as a colorless oil (1.8 g). LCMS ($M+H^+$): 116.

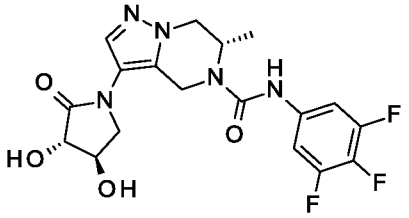
Preparation of (6S)-6-methyl-3-(4-methyl-2-oxo-1,3-oxazinan-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 426)

The title compound was prepared in analogy to **Example 223** by using 4-methyl-1,3-oxazinan-2-one (compound **426c**) instead of pyrrolidin-2-one and phenyl N-(3,4,5-trifluorophenyl)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 426** was obtained as a white solid (26 mg).

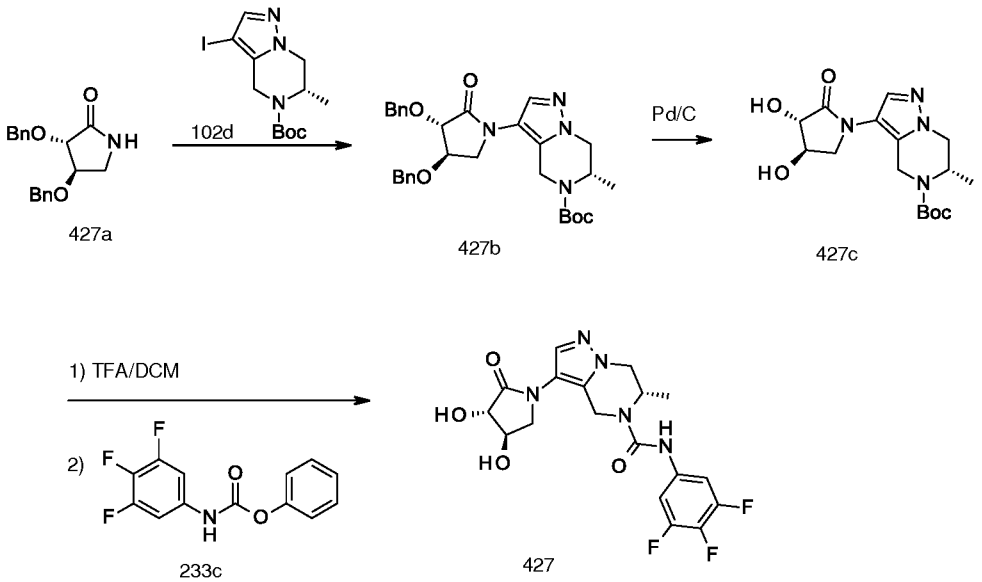
LCMS ($M+H^+$): 424. ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.59-7.22 (m, 2H), 7.16-7.01(m, 2H), 5.07-4.58 (m, 2H), 4.47-3.84 (m, 6H), 2.38-2.28 (m, 1H), 1.95-1.84(m, 1H), 1.34-1.01(m, 6H).

Example 427:

(6S)-3-[(3S,4R)-3,4-dihydroxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of tert-butyl (6S)-3-[(3S,4R)-3,4-dihydroxy-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 427c):

Step 1: To a mixture of tert-butyl (6S)-3-iodo-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound **102d**, 1g, 2.75 mmol), (3S,4R)-3,4-bis(benzyloxy)pyrrolidin-2-one (819 mg, 2.75 mmol, synthesis refers to: J. Org. Chem. 2014, 79, 10487−10503, starting from dimethyl (2S,3S)-2,3-dihydroxybutanedioate), (1R,2R)-N1,N2-dimethylcyclohexane-1,2-diamine (157 mg, 1.1 mmol, 0.4 eq.) and K_3PO_4 (877 mg, 4.13 mmol) in DMSO (15 mL) was added CuI (210 mg, 1.1 mmol) under N_2. The resulting mixture was stirred under microwave for 2 hours at 115 °C. The reaction mixture was diluted by water, extracted with EtOAc (50 mL) two times. The combined organic layer was dried over Na_2SO_4,

and concentrated. The crude material was purified by flash chromatography (silica gel, 10% to 60% EtOAc in hexanes) to give compound **427b** as a colorless oil (1.2 g). LCMS ($M+H^+$): 533.

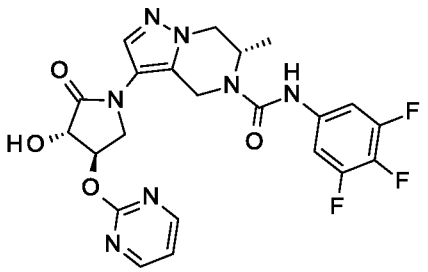
Step 2: A suspension of (S)-tert-butyl 3-((3S,4R)-3,4-bis(benzyloxy)-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (1.2 g, 2.25 mmol) and palladium on carbon (240 mg) in MeOH (50 mL) was heated to 60 °C and stirred for 12 hours under 1 atm of hydrogen. The reaction mixture was filtered and the filtrate was concentrated to give compound **427c** as a white solid (700 mg). LCMS ($M+H^+$): 353.

Preparation of (6S)-3-[(3S,4R)-3,4-dihydroxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 427):

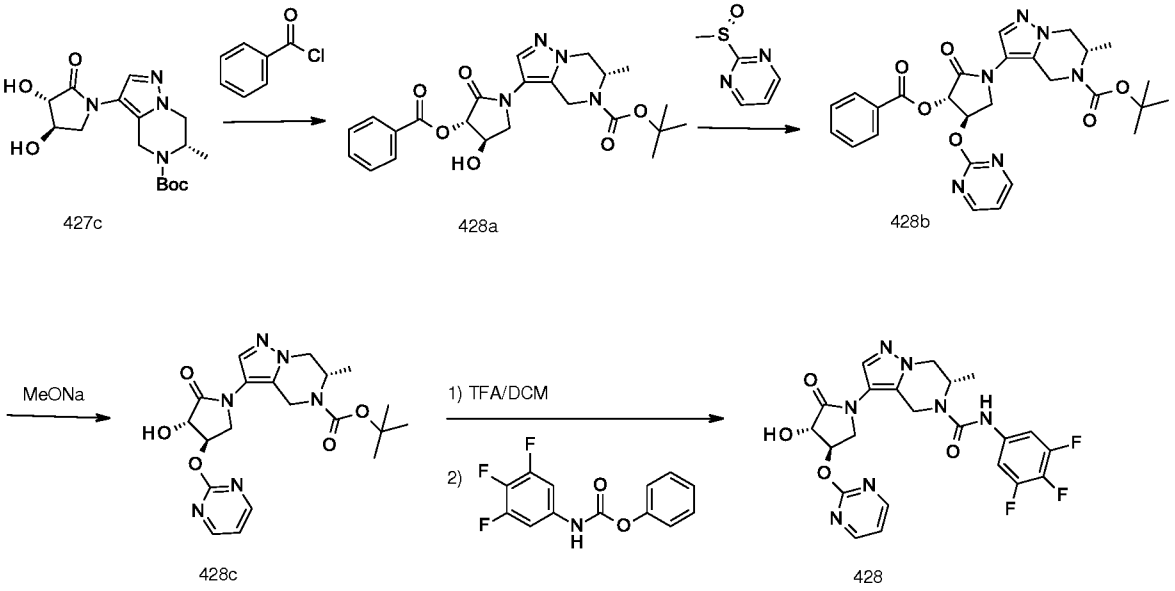
A mixture of (S)-tert-butyl 3-((3S,4R)-3,4-dihydroxy-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **427c**, 30 mg, 85.1 μmol) in TFA (1 mL) and DCM (1 mL) was stirred at rt for 30 mins, and then concentrated. The residue was dissolved in DMF (1 mL), to it was added N-ethyl-N-isopropylpropan-2-amine (55 mg, 426 μmol) and phenyl (3,4,5-trifluorophenyl)carbamate (compound **233c**, 27.3 mg, 102 μmol). The reaction mixture was stirred at 70 °C for 0.5 hours. Then the reaction mixture purified by prep-HPLC to give **Example 427** as a white solid (10 mg). LCMS ($M+H^+$): 426. ^{1}H NMR (400 MHz, METHANOL-d_4) δ ppm 7.64 (s, 1H) 7.31-7.27 (m, 2H) 4.93 - 5.06 (m, 2H) 4.57 (d, J=16.99 Hz, 1H) 4.21 - 4.37 (m, 3H) 4.12 - 4.19 (m, 1H) 3.92 (dd, J=9.54, 7.34 Hz, 1H) 3.59 (dd, J=9.66, 6.72 Hz, 1H) 1.28 (d, J=6.85 Hz, 3H).

Example 428:

(6S)-3-[(3S,4R)-3-hydroxy-2-oxo-4-pyrimidin-2-yloxy-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of tert-butyl (6S)-3-[(3S,4R)-3-hydroxy-2-oxo-4-pyrimidin-2-yloxy-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (compound 428c):

Step 1: To a mixture of (S)-tert-butyl 3-((3S,4R)-3,4-dihydroxy-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **427c**, 400 mg, 1.14 mmol) and pyridine (269 mg, 3.41 mmol) in DCM (10 mL) was added benzoyl chloride (319 mg, 2.27 mmol) slowly. The reaction mixture was stirred at room temperature for 10 minutes and then concentrated. The crude material was purified by flash chromatography (silica gel, 12 g, 20% to 100% EtOAc in hexanes) to give compound **428a** as a white solid (350 mg). LCMS ($M+H^+$): 457.

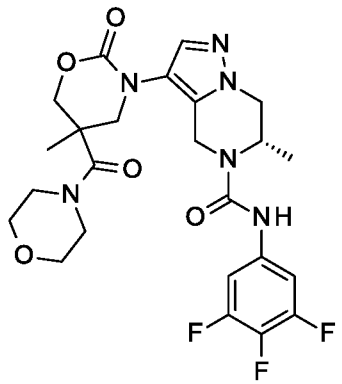
Step 2: To a 20 mL vial was added (S)-tert-butyl 3-((3S,4R)-3-(benzoyloxy)-4-hydroxy-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **428a**, 300 mg, 0.66 mmol), 2-(methylsulfinyl)pyrimidine (140 mg, 1.0 mmol), sodium carbonate (139 mg, 1.3 mmol) and dioxane (10 mL). The vial was sealed and heated at 90 °C for 2 hours. The crude reaction mixture was concentrated in *vacuo*. The crude material was purified by flash chromatography (silica gel, 12 g, 20% to 80% EtOAc in hexanes) to give compound **428b** as a white solid (250 mg). LCMS ($M+H^+$): 535.

Step 3: A mixture of (S)-tert-butyl 3-((3S,4R)-3-(benzoyloxy)-2-oxo-4-(pyrimidin-2-yloxy)pyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **428b**, 250 mg) and sodium methanolate (126 mg) in MeOH (20 mL) was stirred at room temperature for 3 hours, and then concentrated in *vacuo*. The crude material was purified by flash chromatography (silica gel, 12 g, 10% to 70% EtOAc in hexanes, EtOAc contain 10% MeOH) to give compound **428c** as a colorless oil (150 mg)_. LCMS ($M+H^+$): 431.

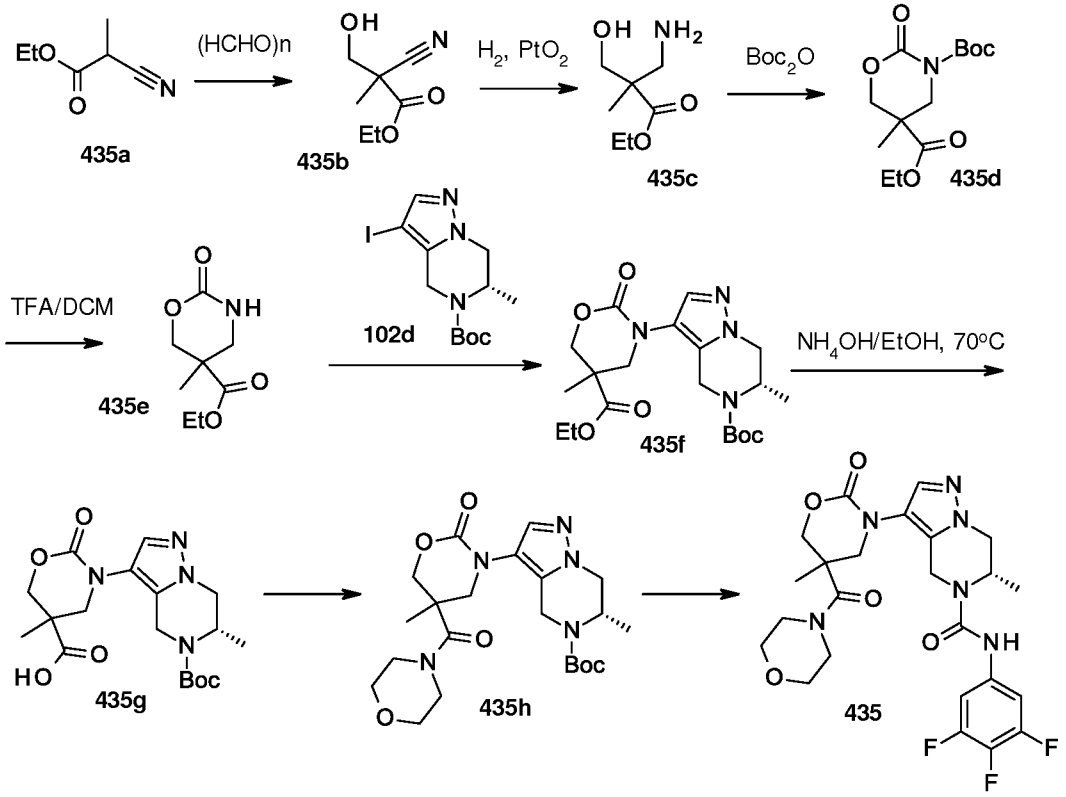
Preparation of (6S)-3-[(3S,4R)-3-hydroxy-2-oxo-4-pyrimidin-2-yloxy-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 428):

The title compound was prepared in analogy to **Example 427** by using tert-butyl (6S)-3-[(3S,4R)-3-hydroxy-2-oxo-4-pyrimidin-2-yloxy-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxylate (**compound 428c**) instead of (S)-tert-butyl 3-((3S,4R)-3,4-dihydroxy-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **427c**). **Example 428** was obtained as a white solid (65 mg). LCMS ($M+H^+$): 504. ^{1}H NMR (400MHz, METHANOL-d_4) δ ppm 8.64 (d, *J*=4.8 Hz, 2H), 7.67 (s, 1H), 7.35 - 7.24 (m, 2H), 7.20 (t, *J*=4.9 Hz, 1H), 5.53 (td, *J*=6.1, 7.3 Hz, 1H), 5.07 (d, *J*=17.0 Hz, 1H), 5.02 - 4.94 (m, 1H), 4.70 (d, *J*=6.2 Hz, 1H), 4.60 (d, *J*=16.9 Hz, 1H), 4.38 (dd, *J*=7.5, 10.3 Hz, 1H), 4.30 (dd, *J*=4.4, 12.7 Hz, 1H), 4.22 - 4.12 (m, 1H), 3.83 (dd, *J*=5.9, 10.2 Hz, 1H), 1.28 (d, *J*=6.8 Hz, 3H)

Example 435:
(6S)-6-methyl-3-[5-methyl-5-(morpholine-4-carbonyl)-2-oxo-1,3-oxazinan-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Step 1: **preparation of ethyl 2-cyano-3-hydroxy-2-methyl-propanoate (compound 435b)**

To a solution of ethyl 2-cyanopropanoate (compound **435a**, 40.0 g, 314.6 mmol) in ethanol (400.0 mL) was added K_2CO_3 (124.4 g, 943.8 mmol) and formaldehyde (14.2 g, 471.9 mmol). The reaction mixture was stirred at 25 °C for 12 h. The reaction mixture was filtered and the filtrate was concentrated. The residue was dissolved in EA, and washed with brine. The organic phase was separated and concentrated. The residue was purified by silica gel column to give compound **435b** as colorless oil (16 g). LCMS ($M+H^+$): 158.

Step 2: preparation of ethyl 2-(aminomethyl)-3-hydroxy-2-methyl-propanoate (compound 435c)

To a solution of ethyl 2-cyano-3-hydroxy-2-methyl-propanoate (compound **435b**, 16.0 g, 101.8 mmol) in ethanol (200.0 mL) was added platinum oxide (2.3 g, 10.2 mmol) and HCl solution (4 M in dioxane, 50.9 mL, 203.6 mmol). The reaction mixture was stirred at 25 °C for 12 hours under H_2 (50 psi) atmosphere. The reaction mixture was filtered and the filtrate was concentrated to give compound **435c** as colorless oil (19.4 g). LCMS ($M+H^+$): 162.

Step 3: preparation of O3-tert-butyl O5-ethyl 5-methyl-2-oxo-1,3-oxazinane-3,5-dicarboxylate (compound 435d)

To a solution of ethyl 2-(aminomethyl)-3-hydroxy-2-methyl-propanoate (compound **435c**, 19.0 g, 96.1 mmol) in acetonitrile (200.0 mL) was added K_2CO_3 (26.6 g, 192.2 mmol). After stirring at 25 °C for 30 minutes, the mixture was added into a stirring mixture of Boc2O (62.9 g, 288.4 mmol), Et3N (29.2 g, 288.4 mmol) and DMAP (2.4 g, 19.2 mmol) in acetonitrile (200 mL). The resulting reaction mixture was stirred for 12 h at 25 °C, and then filtered. The filtrate was concentrated, and the obtained residue was partitioned between H_2O (500 mL) and EtOAc (500 mL). The EtOAc phase was washed with brine (300 mL), concentrated and the residue was purified by column chromatography (PE/EtOAc=3/1) to give compound **435d** as a colorless oil (11 g). LCMS ($M+H^+$): 288.

Step 4: preparation of ethyl 5-methyl-2-oxo-1,3-oxazinane-5-carboxylate (compound 435e)

To a solution of compound O3-tert-butyl O5-ethyl 5-methyl-2-oxo-1,3-oxazinane-3,5-dicarboxylate (compound **435d**, 11.0 g, 38.3 mmol) in DCM (70 mL) was added TFA (14 mL). after being stirred at 25 °C for 2 hours, the reaction mixture was basified to pH 10 by adding sodium hydroxide solution (2.0 M, aqueous). The mixture was then partitioned between H_2O (400 mL) and DCM (400 mL). The DCM phase was washed with brine (200 mL), and then concentrated to give crude compound **435e** (4.2 g). LCMS ($M+H^+$): 188.

Step 5: preparation of ethyl 3-((S)-5-(tert-butoxycarbonyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)-5-methyl-2-oxo-1,3-oxazinane-5-carboxylate (compound 435f)

A mixture of ethyl 5-methyl-2-oxo-1,3-oxazinane-5-carboxylate (compound **435e**, 515 mg, 2.75 mmol) , (S)-tert-butyl 3-iodo-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **102d**, 1.0 g, 2.75 mmol), K_3PO_4 (1.17 g, 5.51 mmol), CuI (105 mg, 0.55 mmol) and (1R,2R)-N1,N2-dimethylcyclohexane-1,2-diamine (78.3 mg, 0.55 mmol) in DMSO (16 mL) was flushed with N_2 and sealed. The reaction mixture was heated to 105 °C in microwave for 2 hours. The reaction mixture was cooled down, diluted with DCM, and then washed with ice-water. The aqueous phase was extracted with DCM/i-PrOH (v/v=5/1) twice. The combined organic layer was dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by silica gel column to give compound **435f** (0.63 g). LCMS ($M+H^+$): 423.

Step 6: preparation of 3-((S)-5-(tert-butoxycarbonyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)-5-methyl-2-oxo-1,3-oxazinane-5-carboxylic acid (compound 435g)

To a solution of ethyl 3-((S)-5-(tert-butoxycarbonyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)-5-methyl-2-oxo-1,3-oxazinane-5-carboxylate (compound **435f**, 0.6 g, 1.42 mmol) in ethanol (8.0 mL) was added 25%- 28% ammonia aqueous solution (8 mL). The reaction mixture was sealed and heated to 70°C overnight. The reaction mixture was concentrated and 2-methyltetrahydrofuran was added to azeotropically remove residue water to give compound **435g** (0.5 g). LCMS ($M+H^+$): 395.

Step 7: preparation of (6S)-tert-butyl 6-methyl-3-(5-methyl-5-(morpholine-4-carbonyl)-2-oxo-1,3-oxazinan-3-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 435h)

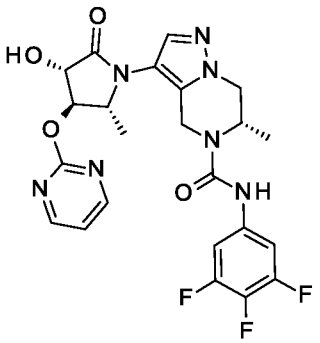
To a solution of 3-((S)-5-(tert-butoxycarbonyl)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)-5-methyl-2-oxo-1,3-oxazinane-5-carboxylic acid (compound **435g**, 78.9 mg, 0.2 mmol) in DCE (3.0 mL) was added morpholine (26.1 mg, 26 μL, 300 μmol), DIPEA (151 mg, 0.2 mL, 1.17 mmol) and HATU (114 mg, 300 μmol). The reaction mixture was stirred at 50 °C for 2 hours. The reaction mixture was cooled down, washed with ice-water, and aqueous phase was extracted with DCM twice. The organic phase was combined, dried over Na_2SO_4, filtrated and concentrated. The residue was purified by silica gel column to give compound **435h** (70 mg). LCMS ($M+H^+$): 464.

Step 8: preparation of (6S)-6-methyl-3-[5-methyl-5-(morpholine-4-carbonyl)-2-oxo-1,3-oxazinan-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 435)

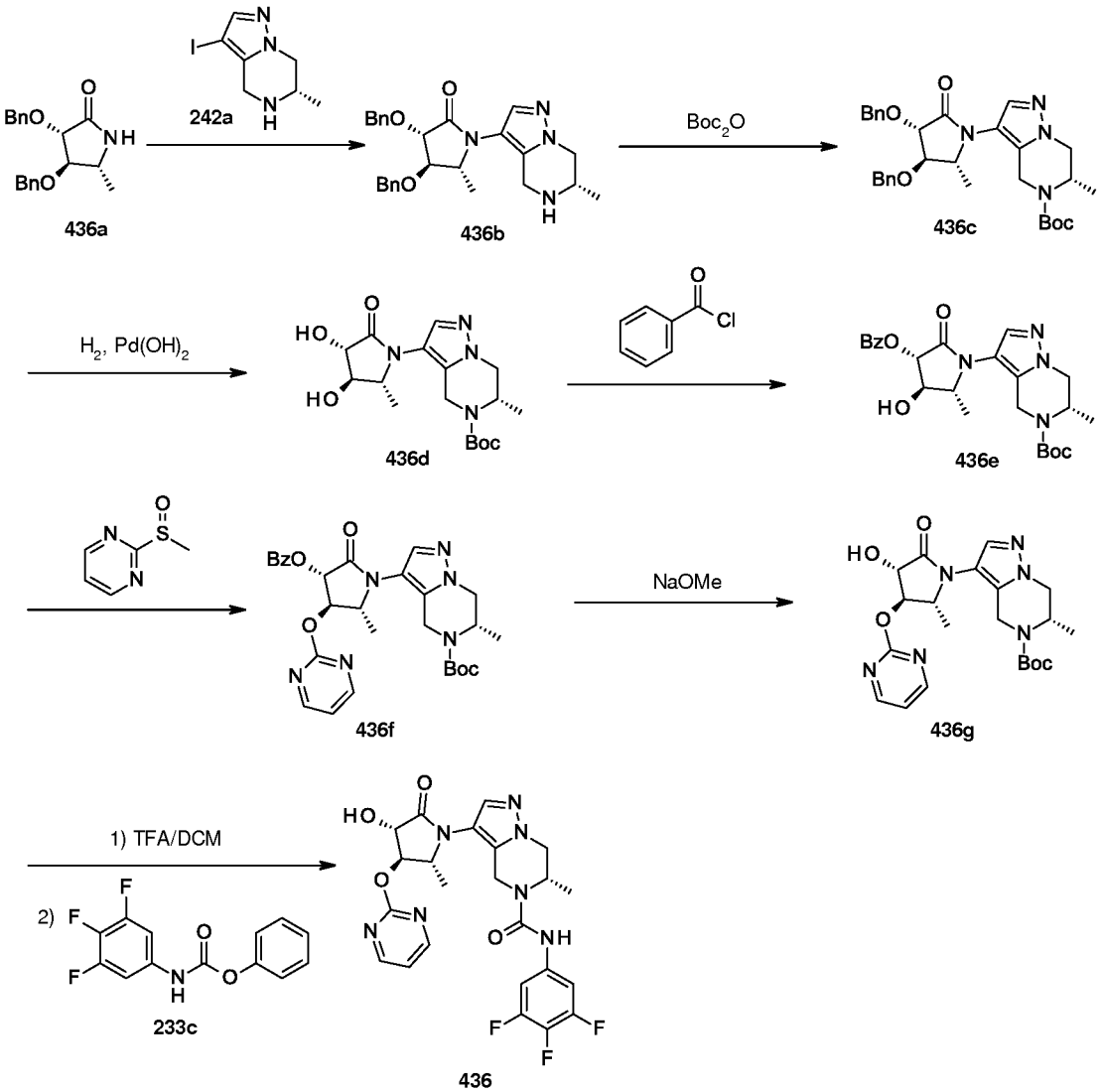
A mixture of (6S)-tert-butyl 6-methyl-3-(5-methyl-5-(morpholine-4-carbonyl)-2-oxo-1,3-oxazinan-3-yl)-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **435h**, 69.5 mg, 0.15 mmol), TFA (2.0 mL) and DCM (1.0 mL) was stirred at room temperature for 1 hour. The reaction mixture was concentrated. The residue was dissolved in DCE (3.0 mL), to it was then added DIPEA (0.5 mL) and phenyl (3,4,5-trifluorophenyl)carbamate (compound **233c**, 60 mg, 225 μmol). The reaction mixture was stirred at 55°C for 2 hours, and then concentrated. The residue was first purified by silica gel column, and then by pre-HPLC to give Example **435** (25 mg). LCMS ($M+H^+$): 537. ^1H NMR (400MHz, CD_3OD) δ ppm 7.67 (s, 0.5H), 7.66 (s, 0.5H), 7.34 - 7.23 (m, 2H), 5.06 - 4.97 (m, 2H), 4.78-4.71 (m, 1H), 4.51 - 4.38 (m, 2H), 4.34-4.26 (m, 1H), 4.19 - 4.12 (m, 1H), 4.11 - 4.02 (m, 1H), 3.74 - 3.65 (m, 9H), 1.45 (s, 1.5H), 1.44 (s, 1.5H), 1.30-1.24 (m, 3H)

Example 436:

(6S)-3-[(2R,3R,4S)-4-hydroxy-2-methyl-5-oxo-3-pyrimidin-2-yloxy-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of (3S,4R,5R)-3,4-bis(benzyloxy)-5-methyl-1-((S)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)pyrrolidin-2-one (compound 436b)

A mixture of (3S,4R,5R)-3,4-bis(benzyloxy)-5-methylpyrrolidin-2-one (compound **436a**, 250 mg, 0.80 mmol, synthesis refers to: Hidemi Yoda et al., *Tetrahedron Letters*, 1996, 37, 5531-5534) , (S)-3-iodo-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazine (compound **242a**, 253 mg, 0.96 mmol), K_3PO_4 (341 mg, 1.61 mmol), CuI (30.6 mg, 0.16 mmol) and (1R,2R)-N1,N2-dimethylcyclohexane-1,2-diamine (22.8 mg, 0.16 mmol) in DMSO (12 mL) was flushed with N_2 and sealed. The reaction mixture was heated at 110 °C in microwave for 2 hours. After cooled down, the reaction mixture was quenched with ice-water, and extracted with EA twice. The combined organic phase was concentrated and the residue was purified by silica gel column to give compound **436b** (251 mg). LCMS ($M+H^+$): 447.

Preparation of (S)-tert-butyl 3-((2R,3R,4S)-3,4-bis(benzyloxy)-2-methyl-5-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 436c)

To a solution of (3S,4R,5R)-3,4-bis(benzyloxy)-5-methyl-1-((S)-6-methyl-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl)pyrrolidin-2-one (compound **436b**, 330 mg, 0.74 mmol) in THF (9.0 mL) and water (3.0 mL) was added sequentially di-tert-butyl dicarbonate (194 mg, 204 μL, 0.89 mmol) and Na_2CO_3 (78.3 mg, 0.74 mmol). The reaction mixture was stirred at room temperature overnight, then extracted with EA twice. The combined organic phase was concentrated, and the residue was purified by silica gel column to give compound **436c** (300 mg) . LCMS ($M+H^+$): 547.

Preparation of (S)-tert-butyl 3-((2R,3R,4S)-3,4-dihydroxy-2-methyl-5-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound 436d)

To a solution of (S)-tert-butyl 3-((2R,3R,4S)-3,4-bis(benzyloxy)-2-methyl-5-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **436c**, 300 mg, 0.55mmol) in EtOH (8.0 mL) was added $Pd(OH)_2$ on carbon. The reaction mixture was stirred at 42 °C for 3 hours under 1 atm of H_2. The reaction mixture was filtrated and concentrated to give crude compound **436d** (200 mg). LCMS ($M+H^+$): 367.

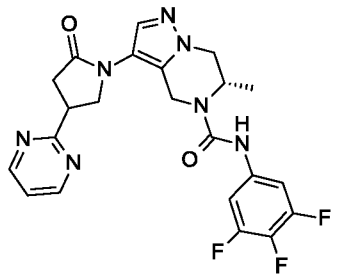
Preparation of (6S)-3-[(2R,3R,4S)-4-hydroxy-2-methyl-5-oxo-3-pyrimidin-2-yloxy-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 436)

The title compound was prepared in analogy to Example **428** by using (S)-tert-butyl 3-((2R,3R,4S)-3,4-dihydroxy-2-methyl-5-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-carboxylate (compound **436d**) instead of (S)-tert-butyl 3-((3S,4R)-3,4-dihydroxy-2-oxopyrrolidin-1-yl)-6-methyl-6,7-dihydropyrazolo[1,5-a]pyrazine-5(4H)-

carboxylate (compound **427c**). Example **436** was obtained as a white solid (23 mg). LCMS ($M+H^+$): 518. ^1H NMR (400MHz, CD_3OD) δ ppm 8.66 (d, *J*=4.9 Hz, 2H), 7.62 (s, 1H), 7.34 - 7.25 (m, 2H), 7.21 (t, *J*=4.8 Hz, 1H), 5.44 (t, *J*=4.8 Hz, 1H), 5.04 - 4.96 (m, 1H), 4.93 (d, *J*=17.0 Hz, 1H), 4.60 - 4.54 (m, 2H), 4.32 (dd, *J*=4.6, 12.8 Hz, 1H), 4.22 - 4.14 (m, 2H), 1.42 (d, *J*=6.5 Hz, 3H), 1.31 (d, *J*=7.0 Hz, 3H).

Example 437:

(6S)-6-methyl-3-(2-oxo-4-pyrimidin-2-yl-pyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide

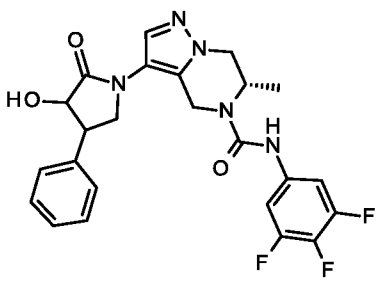


Preparation of (6S)-6-methyl-3-(2-oxo-4-pyrimidin-2-yl-pyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 437)

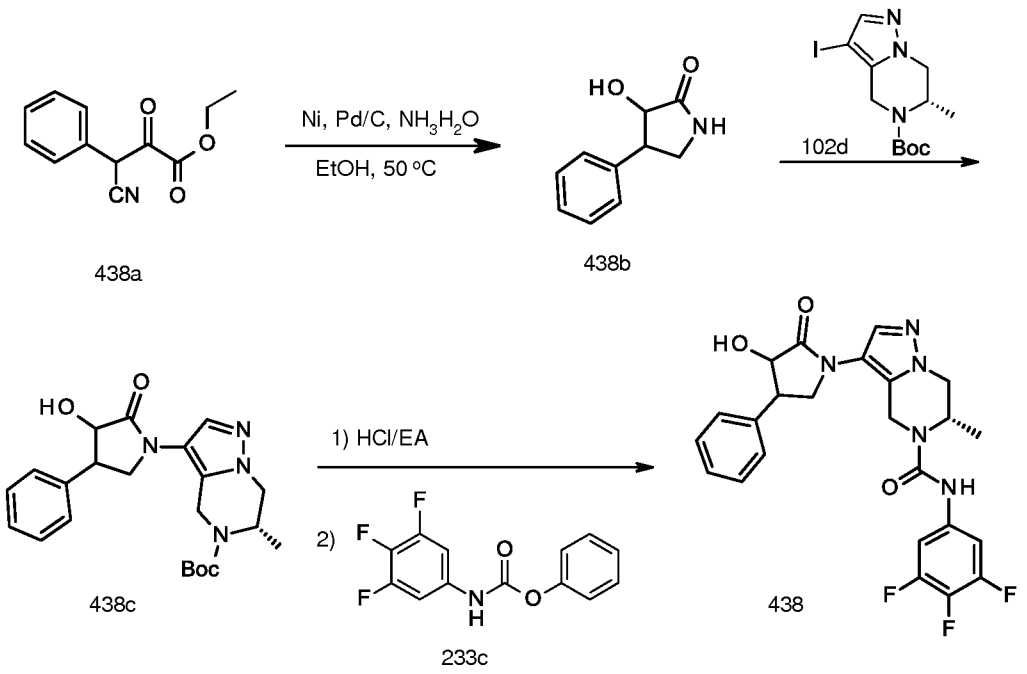
The title compound was prepared in analogy to Example **290** by using pyrimidine-2-carbaldehyde instead of thiazole-5-carbaldehyde. Example **437** was obtained as a white solid (26 mg). LCMS ($M+H^+$): 472. ^1H NMR (400MHz, CD_3OD) δ ppm 8.82 (d, *J*=5.0 Hz, 2H), 7.66 (s, 0.5H), 7.65 (s, 0.5H), 7.43 - 7.38 (m, 1H), 7.34-7.24 (m, 2H), 5.08 (d, *J*=16.9 Hz, 1H), 5.00 - 4.92 (m, 1H), 4.56-4.48 (m, 1H), 4.36 - 4.26 (m, 2H), 4.21 - 4.06 (m, 3H), 3.11 - 2.98 (m, 2H), 1.32-1.24 (m, 3H).

Example 438:

(6S)-3-(3-hydroxy-2-oxo-4-phenyl-pyrrolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of 3-hydroxy-4-phenyl-pyrrolidin-2-one (compound 438b):

To a mixture of ethyl 3-cyano-2-oxo-3-phenyl-propanoate (compound **438a**, 1.5 g, 6.9 mmol) and $NH_3.H_2O$ (0.2 mL) in EtOH (50 mL) was added Raney Ni (2.0 g) and Pd/C (1.0 g). The resulting mixture was stirred at 50 °C for 24 hours under H_2 (50 psi). The reaction mixture was filtered and the filtrate was concentrated. The residue was purified by prep-HPLC to afford cis-enantiomer **438b-1** (100 mg) and trans- enantiomer **438b-2** (50 mg) as white solids. LCMS ($M+H^+$): 178. Cis-enantiomer **438b-1:** ^{1}H NMR (400MHz, DMSO-d^6) δ ppm 7.87 (s, 1H), 7.40-7.15 (m, 5H), 5.43 (d, *J* = 6.0 Hz, 1H), 4.11 (t, *J* = 6.0 Hz, 1H), 3.60-3.40 (m, 2H), 3.38-3.30 (m, 1H); trans-enantiomer **438b-2:** ^{1}H NMR (400MHz, DMSO-d^6) δ ppm 7.85 (s, 1H), 7.45-7.30 (m, 4H), 7.29-7.20 (m, 1H), 5.58 (d, *J* = 6.0 Hz, 1H), 4.15 (dd, *J* = 10, 6.4 Hz, 1H), 3.54-3.44 (m, 1H), 3.27-3.20 (m, 1H), 3.20-3.10 (m, 1H).

Preparation of (6S)-3-(3-hydroxy-2-oxo-4-phenyl-pyrrolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 438):

The title compound was prepared in analogy to **Example 223** by using 3-hydroxy-4-phenyl-pyrrolidin-2-one (compound **438b-1**or **438b-2**) instead of pyrrolidin-2-one and phenyl N-(3,4,5-trifluorophenyl)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 438A** and **Example 438B** were synthesized from cis-enantiomer **438b-1** and separated by chiral SFC; **Example 438C** and **Example 438D** were synthesized from trans-enantiomer **438b-2** and separated by chiral SFC.

Example **438A** (25 mg), white solid. LCMS ($M+H^+$): 486. ^1H NMR (400MHz, MeOD) δ ppm 7.71 (s, 1H), 7.43 - 7.19 (m, 7H), 5.09 (d, *J*=16.9 Hz, 1H), 5.01 - 4.93 (m, 1H), 4.67 - 4.54 (m, 2H), 4.32 (dd, *J*=4.3, 12.7 Hz, 1H), 4.23 - 4.14 (m, 2H), 4.02 (dd, *J*=5.3, 9.9 Hz, 1H), 3.91 - 3.82 (m, 1H), 1.29 (d, *J*=6.9 Hz, 3H).

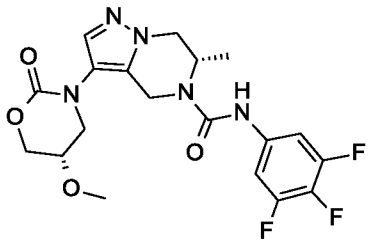
Example **438B** (32 mg), white solid, LCMS ($M+H^+$): 486. ^1H NMR (400MHz, MeOD) δ ppm 7.60 (s, 1H), 7.30 - 7.11 (m, 7H), 5.04 (d, *J*=16.9 Hz, 1H), 4.92 - 4.84 (m, 1H), 4.53 (d, *J*=7.2 Hz, 1H), 4.44 (d, *J*=17.1 Hz, 1H), 4.17 (d, *J*=4.4 Hz, 1H), 4.11 - 4.02 (m, 2H), 3.92 (dd, *J*=5.1, 10.0 Hz, 1H), 3.74 (dt, *J*=5.1, 7.0 Hz, 1H), 1.17 (d, *J*=6.9 Hz, 3H).

Example **438C** (15 mg), white solid. LCMS ($M+H^+$): 486. ^1H NMR (400MHz, MeOD) δ ppm 7.70 (s, 1H), 7.53 - 7.46 (m, 2H), 7.41 (t, *J*=7.5 Hz, 2H), 7.35 - 7.26 (m, 3H), 5.17 (d, *J*=16.8 Hz, 1H), 5.02 - 4.96 (m, 1H), 4.62 (d, *J*=10.2 Hz, 1H), 4.54 (d, *J*=16.9 Hz, 1H), 4.32 (dd, *J*=4.3, 12.9 Hz, 1H), 4.21 - 4.13 (m, 1H), 4.09 - 4.00 (m, 1H), 3.90 (t, *J*=9.7 Hz, 1H), 3.64 - 3.53 (m, 1H), 1.26 (d, *J*=6.9 Hz, 3H).

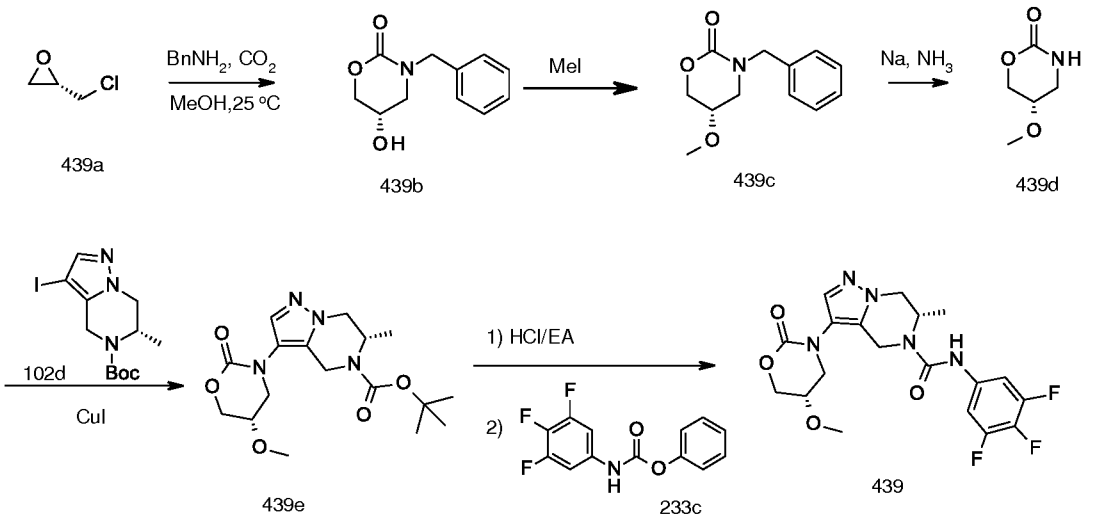
Example **438D** (21 mg), white solid, LCMS ($M+H^+$): 486. ^1H NMR (400MHz, MeOD) δ ppm 7.58 (s, 1H), 7.37 (d, *J*=7.3 Hz, 2H), 7.29 (t, *J*=7.5 Hz, 2H), 7.23 - 7.13 (m, 3H), 4.96 (d, *J*=16.9 Hz, 1H), 4.90 - 4.82 (m, 1H), 4.57 - 4.44 (m, 2H), 4.22 - 4.13 (m, 1H), 4.10 - 4.01 (m, 1H), 3.94 - 3.86 (m, 1H), 3.83 - 3.76 (m, 1H), 3.51 - 3.41 (m, 1H), 1.18 (d, *J*=6.8 Hz, 3H).

Example 439:

(6S)-3-[(5S)-5-methoxy-2-oxo-1,3-oxazinan-3-yl]-6-methyl-N-(3,4,5trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared according to the following scheme:



Preparation of (5S)-5-methoxy-1,3-oxazinan-2-one (compound 439d):

Step 1: A mixture of (2S)-2-(chloromethyl)oxirane (compound **439a**, 60.0 g, 648.5 mmol), $BnNH_2$ (209.0 g, 1945.5 mmol) and MeOH (1.5 L) in 2 L of autoclave was stirred 48 hours under 1 Mpa of CO_2. The reaction was concentrated, and the residue was dissolved in water (200 mL) and acidified by 5N HCl to pH 3~4. The solution was extracted with DCM (300 mLx10). The organic layer was concentrated, and the residue was purified by column chromatography (from PE: EtOAc=2: 1 to DCM: MeOH=10: 1) to give a crude product (15.0 g). The crude product was further purified by prep-HPLC ($NH_3 \cdot H_2O$ as additive) to give compound **439b** as a white solid (5.0 g). LCMS ($M+H^+$): 208. ^1H NMR: (400MHz, $CDCl_3$) δ ppm 7.36 - 7.28 (m, 5H), 4.67 (d, *J*=15.1 Hz, 1H), 4.48 (d, *J*=15.1 Hz, 1H), 4.31 - 4.24 (m, 2H), 4.16 (br. s., 1H), 3.44 (dd, *J*=3.6, 12.2 Hz, 1H), 3.22 (d, *J*=11.5 Hz, 2H).

Step 2: To a solution of (5S)-3-benzyl-5-hydroxy-1,3-oxazinan-2-one (compound **439b**, 450.0 mg, 2.17 mmol) in MeCN (10.0 mL) was added Ag_2O (2.5 g, 10.85 mmol) and MeI (3.0 g, 21.7 mmol). The mixture was stirred at 40 °C for 5 hours. The reaction was filtered and the filtrate was concentrated. The residue was purified by prep-TLC (EtOAc) to give compound **439c** as a white solid (950 mg). LCMS ($M+H^+$): 222. ^1H NMR: (400MHz, MeOD) δ ppm 7.39 - 7.30 (m, 5H), 4.68 (d, *J*=15.3 Hz, 1H), 4.47 - 4.28 (m, 3H), 3.73 (br. s., 1H), 3.49 (dd, *J*=3.3, 12.8 Hz, 1H), 3.37 - 3.32 (m, 1H), 3.30 (s, 3H).

Step 3: NH_3 (gas) was bubbled through a solution of (5S)-3-benzyl-5-methoxy-1,3-oxazinan-2-one (compound **439c**, 400.0 mg, 1.81 mmol) in THF (10.0 mL) at -78 °C for 5 minutes, and then Na (125.0 mg, 5.43 mmol) was added. The mixture was stirred at -78°C for 15 minutes, and then poured into 10 mL aqueous NH_4Cl solution (3.0 g). The resulting mixture was concentrated and the residue was triturated with THF (20 mL). The suspension was filtered and

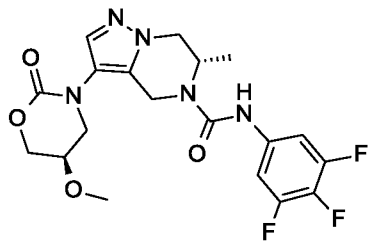
the filtrate was concentrated to give compound **439d** as a colorless oil (100 mg, crude). LCMS ($M+H^+$): 132. ^1H NMR: (400MHz, MeOD) δ ppm 4.29 (td, *J*=2.6, 11.9 Hz, 1H), 4.20 (d, *J*=11.8 Hz, 1H), 3.63 (br. s., 1H), 3.41 - 3.23 (m, 5H).

Preparation of (6S)-3-[(5S)-5-methoxy-2-oxo-1,3-oxazinan-3-yl]-6-methyl-N-(3,4,5trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide (Example 439)

The title compound was prepared in analogy to **Example 223** by using (5S)-5-methoxy-1,3-oxazinan-2-one (compound **439d**) instead of pyrrolidin-2-one and phenyl N-(3,4,5-trifluorophenyl)carbamate (compound **233c**) instead of phenyl N-[2-(difluoromethyl)-4-pyridyl]carbamate (compound **218c**). **Example 439** was obtained as a white solid (8 mg). LCMS ($M+H^+$): 440. ^1H NMR (400MHz, MeOD) δ ppm 7.62 (s, 1H), 7.39 - 7.23 (m, 2H), 4.99 – 4.96 (m, 2H), 4.62 - 4.39 (m, 3H), 4.30 (dd, *J*=4.1, 12.7 Hz, 1H), 4.16 (d, *J*=12.8 Hz, 1H), 4.03 (dd, *J*=2.9, 12.7 Hz, 1H), 3.90 (br. s., 1H), 3.68 (d, *J*=12.8 Hz, 1H), 3.50 (s, 3H), 1.27 (d, *J*=6.8 Hz, 3H).

Example 440:

(6S)-3-[(5R)-5-methoxy-2-oxo-1,3-oxazinan-3-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide



The title compound was prepared in analogy to **Example 439** by using (2R)-2-(chloromethyl)oxirane instead of (2S)-2-(chloromethyl)oxirane. **Example 440** was obtained as a white solid (29 mg). LCMS ($M+H^+$): 440. ^1H NMR (400MHz, MeOD) δ ppm 7.60 (s, 1H), 7.31 - 7.23 (m, 2H), 5.05 – 4.90 (m, 2H), 4.60 - 4.43 (m, 2H), 4.37 (d, *J*=16.8 Hz, 1H), 4.27 (d, *J*=12.8 Hz, 1H), 4.14 (d, *J*=12.8 Hz, 1H), 3.98 (d, *J*=12.4 Hz, 1H), 3.88 (s., 1H), 3.69 (d, *J*=12.4 Hz, 1H), 3.49 (s, 3H), 1.23 (d, *J*=6.8 Hz, 3H).

Example 441: HBV inhibition assays

Cell line and culture conditions:

HepG2.2.15 is a stably-transfected cell line containing the HBV genome. It is derived from the hepatoblastoma cell line Hep G2 (American Type Culture Collection, ATCC® HB-8065™) by the published procedures described in reference: MA Selles *et al.* Proc. Natl. Acad. Sci. USA 1987, 84, 1005-1009. The cell line was maintained in Dulbecco's modified Eagle's medium (DMEM)-F12 medium supplemented with 10% fetal bovine serum, 100 U/mL penicillin, 100 μg/mL streptomycin, and 0.5 mg/mL of G418.

Anti-HBV activity in vitro:

HepG2.2.15 cells were seeded into 96-well plates (3×10^4 cells in 100 μL media per well) and incubated overnight at 37 °C. The test compounds were serially half-log diluted in DMSO, then diluted 100 times in culture media. 100 μL diluted compounds were added into the plates to reach 0.5% final concentration of DMSO in every well. Five days after compound treatment, culture supernatant was collected for further analysis.

For quantitative PCR detection of extracellular HBV DNA, culture supernatant was processed by Proteinase K digestion. After heat inactivation of the enzyme, the samples were subjected to HBV DNA quantification by qPCR. The effective compound concentration at which HBV replication is inhibited by 50% (EC_{50}) was determined.

The Examples of the present invention were tested in the above assays as described herein and found to have EC_{50} of about 0.009 μM to about 3 μM in HepG2.2.15 assay. Particular compounds of the present invention were found to have EC50 below 0.1 μM as shown in Table 1 below.

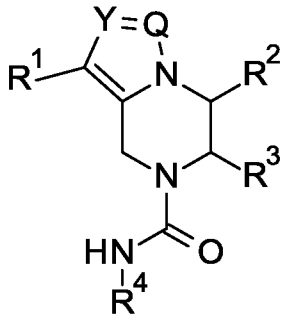
Table 1. Activity of compounds of this invention in HepG2.2.15 assay

Example No	EC_{50} (μM)	Example No	EC_{50} (μM)	Example No	EC_{50} (μM)	Example No	EC_{50} (μM)
21	0.076	**204**	0.036	**290**	0.011	**377**	0.081
24	0.033	**212**	0.033	**291**	0.007	**378**	0.028
30	0.072	**215**	0.100	**292**	0.048	**379**	0.038
33	0.085	**218**	0.014	**294**	0.013	**381**	0.005
34	0.052	**229**	0.047	**295**	0.033	**382**	0.016
50	0.036	**230**	0.052	**296**	0.030	**386**	0.088
51	0.068	**231**	0.025	**297**	0.068	**390**	0.103
53	0.034	**232**	0.049	**298**	0.104	**391**	0.074
61	0.029	**233**	0.076	**299**	0.080	**392**	0.088

67	0.029	**235**	0.039	**302**	0.020	**393**	0.070
68	0.075	**237**	0.074	**303**	0.081	**394**	0.065
73	0.045	**238**	0.021	**309**	0.005	**395**	0.088
76	0.095	**239**	0.038	**318**	0.045	**396**	0.058
78	0.029	**240**	0.016	**321**	0.047	**397**	0.060
79	0.028	**240-1**	0.055	**326**	0.046	**398**	0.080
81	0.032	**240-2**	0.009	**329**	0.004	**399**	0.019
85	0.011	**241**	0.075	**331**	0.012	**400**	0.094
86	0.066	**243**	0.031	**332**	0.011	**401**	0.088
92	0.013	**245**	0.053	**333**	0.046	**403**	0.031
94	0.033	**247**	0.014	**334**	0.022	**404**	0.042
96	0.072	**248**	0.093	**336**	0.066	**405**	0.010
99	0.024	**249**	0.099	**337**	0.015	**406**	0.006
100	0.061	**250**	0.021	**338**	0.014	**407**	0.024
102	0.014	**251**	0.045	**341**	0.040	**408**	0.022
122	0.093	**252**	0.015	**342**	0.041	**409**	0.016
127	0.086	**253**	0.044	**344**	0.007	**410**	0.037
134	0.085	**254**	0.039	**345**	0.017	**411**	0.018
135	0.023	**255**	0.028	**346**	0.012	**412**	0.021
136	0.056	**256**	0.068	**348**	0.094	**413**	0.076
138	0.037	**257**	0.015	**349**	0.015	**414**	0.017
139	0.046	**259**	0.023	**350**	0.015	**415**	0.025
142	0.056	**261**	0.040	**351**	0.012	**419**	0.071
150	0.058	**262**	0.065	**352**	0.014	**420-1**	0.027
155	0.040	**267**	0.039	**353**	0.005	**420-2**	0.030
156	0.025	**268**	0.096	**354**	0.013	**420-3**	0.003
157	0.083	**269**	0.012	**355**	0.036	**421**	0.014
158	0.044	**270**	0.017	**356**	0.050	**422**	0.065
167	0.015	**271**	0.038	**358**	0.043	**424**	0.044
170	0.046	**272**	0.104	**360**	0.043	**425**	0.087
171	0.045	**273**	0.039	**361**	0.011	**426**	0.029
174	0.066	**274**	0.040	**362**	0.032	**428**	0.006
176	0.052	**275**	0.064	**363**	0.009	**436**	0.016
178	0.013	**276**	0.006	**364**	0.028	**437**	0.006
183	0.068	**278**	0.027	**368**	0.047	**438-1**	0.010
198	0.030	**281**	0.052	**369**	0.034	**438-2**	0.108
199	0.030	**282**	0.057	**370**	0.028	**438-3**	0.044
200	0.038	**283**	0.047	**371**	0.020	**438-4**	0.010
201	0.013	**284**	0.010	**372**	0.050		
202	0.051	**285**	0.007	**373**	0.022		
203	0.097	**286**	0.026	**376**	0.088		

CLAIMS

1. A compound of formula (I),



(I),

wherein

R^1 is heterocyclyl, said heterocyclyl being unsubstituted or substituted with one, two or three substituents independently selected from $(C_{1-6}alkyl)_2$aminocarbonyl, $(C_{1-6}alkyl)_2$morpholinylcarbonyl, C_{1-6}alkoxy, C_{1-6}alkoxyC_{1-6}alkyl, C_{1-6}alkoxycarbonyl, C_{1-6}alkyl, C_{1-6}alkyl(C_{1-6}alkylsulfonyl)amino, C_{1-6}alkylaminocarbonyl, C_{1-6}alkylcarbonyl, C_{1-6}alkylcarbonylamino, C_{1-6}alkylimidazolyl, C_{1-6}alkylmorpholinylcarbonyl, C_{1-6}alkyloxadiazolyl, C_{1-6}alkyloxazolyl, C_{1-6}alkylpyrazolyl, C_{1-6}alkylsulfonyl, C_{1-6}alkylsulfonylamino, C_{1-6}alkylsulfonylC_{1-6}alkyl, carbamoyl, cyano, dioxopyrrolidinyl, haloC_{1-6}alkyl, haloC_{1-6}alkyloxadiazolyl, halogen, halopiperidinylcarbonyl, halopyridinyl, halopyrimidinylamino, halopyrimidinyloxy, halopyrrolidinylcarbonyl, hydroxy, hydroxyazetidinylcarbonyl, hydroxyC_{1-6}alkyl, hydroxyC_{1-6}alkyl(C_{1-6}alkyl)aminocarbonyl, hydroxyC_{1-6}alkylaminocarbonyl, hydroxypyrrolidinylcarbonyl, morpholinylcarbonyl, oxadiazolyl, oxazolyl, oxazolylaminocarbonyl, oxazolyl(C_{1-6}alkyl)aminocarbonyl, oxazolylcarbonyl, oxazolylcarbonyl(C_{1-6}alkyl)amino, oxomorpholinyl, oxooxazolidinyl, oxopyrrolidinyl, phenyl, phenylcarbonyl, pyrazolylC_{1-6}alkyl, pyridinyl, pyrimidinyl, pyrimidinylamino, pyrimidinyl(C_{1-6}alkyl)amino, pyrimidinyloxy, pyrimidinyloxyC_{1-6}alkyl, pyrrolidinylcarbonyl and thiazolyl;

heteroaryl, said heteroaryl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, C_{1-6}alkyl ,haloC_{1-6}alkyl, hydroxy C_{1-6}alkyl and C_{1-6}alkoxyC_{1-6}alkyl;

phenyl, said phenyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, hydroxy, C_{1-6}alkyl, C_{1-6}alkoxy, C_{3-7}cycloalkyl, haloC_{1-6}alkoxy and haloC_{1-6}alkyl; or

C_{3-7}cycloalkyl;

R^2 and R^3 are independently selected from hydrogen and C_{1-6}alkyl;

R^4 is heteroaryl, said heteroaryl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, C_{1-6}alkyl, haloC_{1-6}alkyl, C_{1-6}alkoxy, C_{3-7}cycloalkyl and $(C_{1-6}alkyl)_2$amino;

aryl, said aryl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, C_{3-7}cycloalkyl, C_{1-6}alkyl, C_{2-6}alkynyl, C_{1-6}alkoxy, haloC_{1-6}alkyl and haloC_{1-6}alkoxy;

phenylC_{1-6}alkyl, said phenylC_{1-6}alkyl being unsubstituted or substituted with one, two or three halogen; or

C_{3-7}cycloalkyl;

Y and Q are independently selected from CH and N;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

2. A compound of formula (I) according to claim 1, wherein

R^1 is azabicyclo[3.1.0]hexanyl;

dioxopiperazinyl;

dioxopyrimidinyl;

dioxotetrahydropyrrolo[1,2-a]pyrazinyl;

morpholinyl, said morpholinyl being unsubstituted or substituted with one, two or three C_{1-6}alkyl;

oxaazabicyclo[3.2.1]octanyl;

oxoazabicyclo[3.1.0]hexanyl;

oxoazaspiro[2.4]heptanyl, said oxoazaspiro[2.4]heptanyl being unsubstituted or substituted with hydroxy;

oxoazaspiro[4.4]nonanyl;

oxoazaspiro[3.4]octanyl, said oxoazaspiro[3.4]octanyl being unsubstituted or substituted with hydroxy;

oxodiazaspiro[3.4]octanyl, said oxodiazaspiro[3.4]octanyl being unsubstituted or substituted with one, two or three substituents independently selected from C_{1-6}alkylcarbonyl, C_{1-6}alkoxycarbonyl, oxazolylcarbonyl and pyrimidinyl;

oxodihydropyrazolo[1,5-a]pyrazinyl;

oxohexahydropyrimidinyl;

oxoimidazolidinyl, said oxoimidazolidinyl being unsubstituted or substituted with one, two or three substituents independently selected from C_{1-6}alkyl, C_{1-6}alkylcarbonyl, C_{1-6}alkylsulfonyl, phenyl, phenylcarbonyl and pyrimidinyl;

oxoindolinyl;

oxoisoindolinyl;

oxomorpholinyl, said oxomorpholinyl being unsubstituted or substituted with one, two or three substituents independently selected from C_{1-6}alkyl and oxazolyl;

oxooxaazaspiro[2.4]heptanyl;

oxooxaazaspiro[3.4]octanyl;

oxooxaazaspiro[4.4]nonanyl;

oxooxaazaspiro[4.5]decanyl;

oxooxazinanyl, said oxooxazinanyl being unsubstituted or substituted with one, two or three substituents independently selected from C_{1-6}alkyl, C_{1-6}alkoxy and morpholinylcarbonyl;

oxooxazolidinyl, said oxooxazolidinyl being unsubstituted or substituted with one, two or three substituents independently selected from C_{1-6}alkyl, phenyl, pyridinyl, halopyridinyl, oxazolyl, C_{1-6}alkylimidazolyl and C_{1-6}alkyloxadiazolyl;

oxopiperidyl, said oxopiperidyl being unsubstituted or substituted with one, two or three substituents independently selected from C_{1-6}alkyl and hydroxy;

oxopyrrolidinyl, said oxopyrrolidinyl being unsubstituted or substituted with one, two or three substituents independently selected from $(C_{1-6}alkyl)_2$aminocarbonyl, $(C_{1-6}alkyl)_2$morpholinylcarbonyl, C_{1-6}alkoxy, C_{1-6}alkoxyC_{1-6}alkyl, C_{1-6}alkyl, C_{1-6}alkyl(C_{1-6}alkylsulfonyl)amino, C_{1-6}alkylaminocarbonyl, C_{1-6}alkylcarbonylamino, C_{1-6}alkylmorpholinylcarbonyl, C_{1-6}alkyloxadiazolyl, C_{1-6}alkyloxazolyl, C_{1-6}alkylpyrazolyl, C_{1-6}alkylsulfonyl, C_{1-6}alkylsulfonylamino, C_{1-6}alkylsulfonylC_{1-6}alkyl, cyano, dioxopyrrolidinyl, haloC_{1-6}alkyl, haloC_{1-6}alkyloxadiazolyl, halopiperidinylcarbonyl,

halopyrimidinylamino, halopyrimidinyloxy, halopyrrolidinylcarbonyl, hydroxy, hydroxyazetidinylcarbonyl, hydroxyC_{1-6}alkyl, hydroxyC_{1-6}alkyl(C_{1-6}alkyl)aminocarbonyl, hydroxyC_{1-6}alkylaminocarbonyl, hydroxypyrrolidinylcarbonyl, morpholinylcarbonyl, oxadiazolyl, oxazolyl, oxazolylaminocarbonyl, oxazolyl(C_{1-6}alkyl)aminocarbonyl, oxazolylcarbonyl(C_{1-6}alkyl)amino, oxomorpholinyl, oxooxazolidinyl, oxopyrrolidinyl, phenyl, pyrazolylC_{1-6}alkyl, pyridinyl, pyrimidinyl, pyrimidinylamino, pyrimidinylC_{1-6}alkylamino, pyrimidinyloxy, pyrimidinyloxyC_{1-6}alkyl, pyrrolidinylcarbonyl and thiazolyl;

oxopyrrolo[3,2-c]pyridinyl;

oxopyrrolo[3,4-b]pyridinyl;

oxotetrahydrofuro[3,4-c]pyrrolyl;

oxotetrahydroimidazo[5,1-c][1,4]oxazinyl;

piperidinyl, said piperidinyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, hydroxy and C_{1-6}alkylcarbonyl;

pyrazolyl, said pyrazolyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, C_{1-6}alkyl, hydroxyC_{1-6}alkyl and C_{1-6}alkoxyC_{1-6}alkyl;

pyridinyl, said pyridinyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, C_{1-6}alkyl and haloC_{1-6}alkyl;

pyrimidinyl, said pyrimidinyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen and C_{1-6}alkyl;

pyrrolidinyl, said pyrrolidinyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, hydroxy, C_{1-6}alkyl, haloC_{1-6}alkyl, C_{1-6}alkoxy and C_{1-6}alkoxyC_{1-6}alkyl;

tetrahydrofuranyl;

thiazolyl, said thiazolyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen and haloC_{1-6}alkyl;

phenyl, said phenyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, hydroxy, C_{3-7}cycloalkyl, C_{1-6}alkyl, C_{1-6}alkoxy, haloC_{1-6}alkyl and haloC_{1-6}alkoxy;or

C_{3-7}cycloalkyl;

R^2 and R^3 are independently selected from hydrogen and C_{1-6}alkyl;

R^4 is benzofuranyl;

benzothiophenyl;

benzoxazolyl;

indolyl;

C_{1-6}alkylbenzothiazolyl;

pyridinyl, said pyridinyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, C_{1-6}alkyl, C_{3-7}cycloalkyl, C_{1-6}alkoxy, haloC_{1-6}alkyl and (C_{1-6}alkyl)$_2$amino;

bicyclo[4.2.0]octa-1(6),2,4-trienyl;

indanyl;

phenyl, said phenyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, C_{3-7}cycloalkyl, C_{1-6}alkyl, C_{2-6}alkynyl, C_{1-6}alkoxy, haloC_{1-6}alkyl and haloC_{1-6}alkoxy;

phenylC_{1-6}alkyl, said phenylC_{1-6}alkyl being unsubstituted or substituted with one, two or three halogen;

or C_{3-7}cycloalkyl;

Y and Q are independently selected from CH and N;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

3. A compound of formula (I) according to claim 1 or 2, wherein

R^1 is pyrazolyl substituted by halogen, cyano, C_{1-6}alkyl, hydroxyC_{1-6}alkyl or C_{1-6}alkoxyC_{1-6}alkyl;

pyridinyl, said pyridinyl being unsubstituted or substituted with one or two substituents independently selected from halogen, cyano, C_{1-6}alkyl and haloC_{1-6}alkyl;

pyrimidinyl substituted with one or two substituents independently selected from halogen and C_{1-6}alkyl;

thiazolyl, said thiazolyl being unsubstituted or substituted by halogen or haloC_{1-6}alkyl;

phenyl, said phenyl being unsubstituted or substituted with one or two substituents independently selected from halogen, cyano, hydroxy, C_{3-7}cycloalkyl, C_{1-6}alkyl, C_{1-6}alkoxy, haloC_{1-6}alkyl and haloC_{1-6}alkoxy;

R^2 and R^3 are independently selected from hydrogen and C_{1-6}alkyl with the proviso that R^2 and R^3 are not C_{1-6}alkyl simultaneously;

R^4 is benzothiophenyl;

benzoxazolyl;

indolyl;

benzothiazolyl substituted by C_{1-6}alkyl;

pyridinyl, said pyridinyl being unsubstituted or substituted with one or two substituents independently selected from halogen, cyano, C_{1-6}alkyl, C_{3-7}cycloalkyl, C_{1-6}alkoxy, haloC_{1-6}alkyl and $(C_{1-6}alkyl)_2$amino;

bicyclo[4.2.0]octa-1(6),2,4-trienyl;

phenyl, said phenyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, C_{3-7}cycloalkyl, C_{1-6}alkyl, C_{2-6}alkynyl, C_{1-6}alkoxy, haloC_{1-6}alkyl and haloC_{1-6}alkoxy;

phenylC_{1-6}alkyl, said phenylC_{1-6}alkyl being unsubstituted or substituted with one or two halogen;

or C_{3-7}cycloalkyl;

Y and Q are independently selected from CH and N;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

4. A compound of formula (I) according to claim 3, wherein

R^1 is fluorophenyl, phenyl, chlorophenyl, trifluoromethylphenyl, cyanophenyl, methoxyphenyl, methylphenyl, difluorophenyl, fluorochlorophenyl, difluoromethylphenyl, methylfluorophenyl, cyclopropylphenyl, hydroxyphenyl, trifluoromethoxyphenyl, bromophenyl, methylpyrazolyl, cyanopyrazolyl, fluoropyrazolyl, hydroxymethylpyrazolyl, methoxymethylpyrazolyl, trifluoromethylpyridinyl, cyanopyridinyl, methylfluoropyridinyl, pyridinyl, chloropyridinyl, fluoropyridinyl, fluorochloropyridinyl, fluoropyrimidinyl, methylfluoropyrimidinyl, thiazolyl, trifluoromethylthiazolyl or chlorothiazolyl;

R^2 and R^3 are independently selected from hydrogen and methyl with the proviso that R^2 and R^3 are not methyl simultaneously;

R^4 is phenyl, trifluoromethylphenyl, fluorochlorophenyl, fluorophenyl, chlorophenyl, cyanophenyl, pyridinyl, methylfluoropyridinyl, fluorotrifluoromethylphenyl, trifluorophenyl, fluorochlorobenzyl, dichlorobenzyl, methylchloropyridinyl, methylbenzothiazolyl, benzothiophenyl, trifluoromethylpyridinyl, difluorophenyl, fluorocyanophenyl, indolyl, methylfluorophenyl, chloropyridinyl, cyanopyridinyl, chloromethoxypyridinyl, methyltrifluoromethylphenyl, chlorotrifluoromethylphenyl, chlorocyanophenyl, ethylphenyl, ethynylphenyl, isopropylphenyl, methoxyphenyl, ethynylfluorophenyl, dimethylpyridinyl, fluorobromophenyl, difluoromethoxyphenyl, fluorotrifluoromethoxyphenyl, difluoromethylphenyl, methylphenyl, difluorocyanophenyl, fluorochloropyridinyl, cyclopropylphenyl, methyldifluorophenyl, difluorochlorophenyl, cyclopropyldifluorophenyl, difluoroethylphenyl, cyclopropylfluorophenyl, methoxydifluorophenyl, benzyl, fluoropyridinyl, benzoxazolyl, methylpyridinyl, difluoropyridinyl, cyclopentyl, cyclohexyl, bicyclo[4.2.0]octa-1(6),2,4-trienyl, bromopyridinyl, cyclopropylpyridinyl, dimethylaminopyridinyl or difluoromethylpyridinyl;

Y and Q are independently selected from CH and N;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

5. A compound of formula (I) according to claim 3 or 4, wherein R^1 is phenyl, said phenyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, hydroxy, C_{3-7}cycloalkyl, C_{1-6}alkyl, C_{1-6}alkoxy, haloC_{1-6}alkyl and haloC_{1-6}alkoxy; or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

6. A compound of formula (I) according to claim 5, wherein R^1 is phenyl, bromophenyl, chlorophenyl, cyanophenyl, cyclopropylphenyl, difluorophenyl, difluoromethylphenyl, fluorophenyl, fluorochlorophenyl, fluoromethylphenyl, hydroxyphenyl, methoxyphenyl, methylphenyl, trifluoromethoxyphenyl or trifluoromethylphenyl; or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

7. A compound of formula (I) according to any one of claims 3 to 6, wherein R^4 is phenyl, said phenyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano, C_{3-7}cycloalkyl, C_{1-6}alkyl, C_{2-6}alkynyl, C_{1-6}alkoxy, haloC_{1-6}alkyl and haloC_{1-6}alkoxy; or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

8. A compound of formula (I) according to claim 7, wherein R^4 is phenyl, chlorophenyl, chlorocyanophenyl, chlorotrifluoromethylphenyl, cyanophenyl, cyclopropylphenyl, difluorophenyl, difluoroethylphenyl, difluoromethoxyphenyl, difluoromethylphenyl, ethylphenyl, ethynylphenyl, fluorophenyl, fluorobromophenyl, fluorochlorophenyl, fluorocyanophenyl, fluorocyclopropylphenyl, fluoroethynylphenyl, difluorochlorophenyl, difluorocyanophenyl, difluorocyclopropylphenyl, methoxydifluorophenyl, methyldifluorophenyl, methylfluorophenyl, fluorotrifluoromethoxyphenyl, fluorotrifluoromethylphenyl, isopropylphenyl, methoxyphenyl, methylphenyl, methyltrifluoromethylphenyl, trifluorophenyl or trifluoromethylphenyl; or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

9. A compound of formula (I) according to claim 3 or 4, wherein

R^1 is pyrazolyl substituted by halogen or hydroxyC_{1-6}alkyl;

pyridinyl substituted by halogen;

pyrimidinyl substituted by halogen;

phenyl substituted once or twice by halogen;

R^2 is H;

R^3 is H or C_{1-6}alkyl;

R^4 is pyridinyl substituted by haloC_{1-6}alkyl; or

phenyl substituted with one, two or three substituents independently selected from halogen and cyano;

Y and Q are independently selected from CH and N, with proviso that Y and Q are not CH simultaneously;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

10. A compound of formula (I) according to claim 9, wherein

R^1 is fluoropyrazolyl, hydroxymethylpyroazolyl, fluoropyridinyl, fluoropyrimidinyl, fluorophenyl or difluorophenyl;

R^2 is H;

R^3 is H or methyl;

R^4 is difluoromethylpyridinyl, fluorochlorophenyl, fluorocyanophenyl or trifluorophenyl;

Y and Q are independently selected from CH and N, with proviso that Y and Q are not CH simultaneously;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

11. A compound according to claim 8 or 9, selected from

N-(3-cyano-4-fluoro-phenyl)-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(5-fluoro-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(5-fluoro-2-pyridyl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-fluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-1-(2,4-difluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

1-(2,4-difluorophenyl)-N-(3,4,5-trifluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(2,4-difluorophenyl)-6,7-dihydro-4H-triazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(4-fluoropyrazol-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-[2-(difluoromethyl)-4-pyridyl]-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(5-fluoropyrimidin-2-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide; and

(6S)-3-[4-(hydroxymethyl)pyrazol-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

12. A compound of formula (I) according to claim 1 or 2, wherein

R^1 is azabicyclo[3.1.0]hexanyl;

morpholinyl, said morpholinyl being unsubstituted or substituted twice by C_{1-6}alkyl;
oxaazabicyclo[3.2.1]octanyl;
piperidinyl, said piperidinyl being unsubstituted or substituted with one or two substituents independently selected from halogen, hydroxy and C_{1-6}alkylcarbonyl;
pyrrolidinyl, said pyrrolidinyl being unsubstituted or substituted with one or two substituents independently selected from halogen, cyano, hydroxy, C_{1-6}alkyl, haloC_{1-6}alkyl, C_{1-6}alkoxy and C_{1-6}alkoxyC_{1-6}alkyl;
tetrahydrofuranyl; or
C_{3-7}cycloalkyl;

R^2 is H;

R^3 is H or C_{1-6}alkyl;

R^4 is benzofuranyl;
pyridinyl, said pyridinyl being substituted with one or two substituents independently selected from halogen and haloC_{1-6}alkyl;
indanyl;
phenyl, said phenyl being unsubstituted or substituted with one, two or three substituents independently selected from halogen, cyano and C_{1-6}alkyl; or
phenylC_{1-6}alkyl;

Y is CH when Q is N; or Y is N when Q is CH;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

13. A compound of formula (I) according to claim 12, wherein

R^1 is azabicyclo[3.1.0]hexanyl, cyclohexyl, cyclopentyl, morpholinyl, dimethylmorpholinyl, oxaazabicyclo[3.2.1]octanyl, piperidinyl, difluoropiperidinyl, hydroxypiperidinyl, acetylpiperidinyl, pyrrolidinyl, methylpyrrolidinyl, methoxymethylpyrrolidinyl, methoxypyrrolidinyl, trifluoromethylpyrrolidinyl, cyanopyrrolidinyl, methylhydroxypyrrolidinyl, difluoropyrrolidinyl or tetrahydrofuranyl;

R^2 is H;

R^3 is H or methyl;

R^4 is benzofuranyl, indanyl, benzyl, phenyl, fluorochlorophenyl, fluorocyanophenyl, trifluorophenyl, methyldifluorophenyl, chloropyridinyl, fluorochloropyridinyl or trifluoromethylpyridinyl;

Y is CH when Q is N; or Y is N when Q is CH;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

14. A compound of formula (I) according to claim 1 or 2, wherein

R^1 is dioxopiperazinyl;

dioxopyrimidinyl

dioxotetrahydropyrrolo[1,2-a]pyrazinyl;

oxoazabicyclo[3.1.0]hexanyl;

oxoazaspiro[2.4]heptanyl, said oxoazaspiro[2.4]heptanyl being unsubstituted or substituted with hydroxy;

oxoazaspiro[4.4]nonanyl;

oxoazaspiro[3.4]octanyl, said oxoazaspiro[3.4]octanyl being unsubstituted or substituted with hydroxy;

oxodiazaspiro[3.4]octanyl, said oxodiazaspiro[3.4]octanyl being substituted by C_{1-6}alkylcarbonyl, C_{1-6}alkoxycarbonyl, oxazolylcarbonyl or pyrimidinyl;

oxodihydropyrazolo[1,5-a]pyrazinyl;

oxohexahydropyrimidinyl;

oxoimidazolidinyl, said oxoimidazolidinyl being unsubstituted or substituted with one or two substituents independently selected from C_{1-6}alkyl, C_{1-6}alkylcarbonyl, C_{1-6}alkylsulfonyl, phenyl, phenylcarbonyl and pyrimidinyl;

oxoindolinyl;

oxomorpholinyl, said oxomorpholinyl being unsubstituted or substituted with one or two substituents independently selected from C_{1-6}alkyl and oxazolyl;

oxooxaazaspiro[2.4]heptanyl;

oxooxaazaspiro[3.4]octanyl;

oxooxaazaspiro[4.4]nonanyl;

oxooxaazaspiro[4.5]decanyl;

oxooxazinanyl, said oxooxazinanyl being unsubstituted or substituted with one or two substituents independently selected from C_{1-6}alkyl, C_{1-6}alkoxy and morpholinylcarbonyl;

oxooxazolidinyl, said oxooxazolidinyl being unsubstituted or substituted with one or two substituents independently selected from C_{1-6}alkyl, phenyl, pyridinyl, halopyridinyl, oxazolyl, C_{1-6}alkylimidazolyl and C_{1-6}alkyloxadiazolyl;

oxopiperidyl substituted by C_{1-6}alkyl or hydroxy;

oxopyrrolidinyl, said oxopyrrolidinyl being unsubstituted or substituted with one, two or three substituents independently selected from $(C_{1-6}alkyl)_2$aminocarbonyl, $(C_{1-6}alkyl)_2$morpholinylcarbonyl, C_{1-6}alkoxy, C_{1-6}alkoxyC_{1-6}alkyl, C_{1-6}alkyl, C_{1-6}alkyl(C_{1-6}alkylsulfonyl)amino, C_{1-6}alkylaminocarbonyl, C_{1-6}alkylcarbonylamino, C_{1-6}alkylmorpholinylcarbonyl, C_{1-6}alkyloxadiazolyl, C_{1-6}alkyloxazolyl, C_{1-6}alkylpyrazolyl, C_{1-6}alkylsulfonyl, C_{1-6}alkylsulfonylamino, C_{1-6}alkylsulfonylC_{1-6}alkyl, cyano, dioxopyrrolidinyl, haloC_{1-6}alkyl, haloC_{1-6}alkyloxadiazolyl, halopiperidinylcarbonyl, halopyrimidinylamino, halopyrimidinyloxy, halopyrrolidinylcarbonyl, hydroxy, hydroxyazetidinylcarbonyl, hydroxyC_{1-6}alkyl, hydroxyC_{1-6}alkyl, hydroxyC_{1-6}alkyl(C_{1-6}alkyl)aminocarbonyl, hydroxyC_{1-6}alkylaminocarbonyl, hydroxypyrrolidinylcarbonyl, morpholinylcarbonyl, oxadiazolyl, oxazolyl, oxazolylaminocarbonyl, oxazolyl(C_{1-6}alkyl)aminocarbonyl, oxazolylcarbonyl(C_{1-6}alkyl)amino, oxomorpholinyl, oxooxazolidinyl, oxopyrrolidinyl, phenyl, pyrazolylC_{1-6}alkyl, pyridinyl, pyrimidinyl, pyrimidinylamino, pyrimidinyl(C_{1-6}alkyl)amino, pyrimidinyloxy, pyrimidinyloxyC_{1-6}alkyl, pyrrolidinylcarbonyl and thiazolyl;

oxopyrrolo[3,2-c]pyridinyl;

oxopyrrolo[3,4-b]pyridinyl;

oxotetrahydrofuro[3,4-c]pyrrolyl;

oxotetrahydroimidazo[5,1-c][1,4]oxazinyl;

R^2 and R^3 are independently selected from hydrogen and C_{1-6}alkyl with the proviso that R^2 is not C_{1-6}alkyl when R^3 is H;

R^4 is pyridinyl substituted with one or two substituents independently selected from halogen and haloC_{1-6}alkyl;

phenyl substituted with one, two or three substituents independently selected from halogen and haloC_{1-6}alkyl;

Y is CH;

Q is N;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

15. A compound of formula (I) according to claim 14, wherein

R^1 is dioxopiperazinyl, dioxopyrimidinyl, dioxotetrahydropyrrolo[1,2-a]pyrazinyl, oxoazabicyclo[3.1.0]hexanyl, oxoazaspiro[2.4]heptanyl, hydroxy oxoazaspiro[2.4]heptanyl, oxoazaspiro[4.4]nonanyl, oxoazaspiro[3.4]octanyl, hydroxyoxoazaspiro[3.4]octanyl, acetyloxodiazaspiro[3.4]octanyl, methoxycarbonyloxodiazaspiro[3.4]octanyl, ethoxycarbonyloxodiazaspiro[3.4]octanyl, oxazolylcarbonyloxodiazaspiro[3.4]octanyl, pyrimidinyloxodiazaspiro[3.4]octanyl, oxodihydropyrazolo[1,5-a]pyrazinyl, oxohexahydropyrimidinyl, oxoimidazolidinyl, acetyloxoimidazolidinyl, benzoyloxoimidazolidinyl, dimethyloxoimidazolidinyl, methyloxoimidazolidinyl, methylsulfonyloxoimidazolidinyl, phenyloxoimidazolidinyl, pyrimidinyloxoimidazolidinyl, oxoindolinyl, oxoisoindolinyl, oxomorpholinyl, methyloxomorpholinyl, dimethyloxomorpholinyl, oxazolyloxomorpholinyl, oxooxaazaspiro[4.5]decanyl, oxooxaazaspiro[4.4]nonanyl, oxooxaazaspiro[2.4]heptanyl, oxooxaazaspiro[3.4]octanyl, oxooxazinanyl, methyloxooxazinanyl, dimethyloxooxazinanyl, methoxyoxooxazinanyl, morpholinylcarbonyl(methyl)oxooxazinanyl, oxooxazolidinyl, dimethyloxooxazolidinyl, chloropyridinyloxooxazolidinyl, fluoropyridinyloxooxazolidinyl, methyloxooxazolidinyl, methylimidazolyloxooxazolidinyl, methyloxadiazolyloxooxazolidinyl, oxazolyloxooxazolidinyl, phenyloxooxazolidinyl, pyridinyloxooxazolidinyl, hydroxyoxopiperidyl, methyloxopiperidyl, oxopyrrolidinyl, acetylaminooxopyrrolidinyl, cyanooxopyrrolidinyl, difluoropiperidinylcarbonyl(methyl)oxopyrrolidinyl, difluoropyrrolidinylcarbonyloxopyrrolidinyl, difluoropyrrolidinylcarbonyl(methyl)oxopyrrolidinyl, dihydroxyoxopyrrolidinyl, dimethyloxopyrrolidinyl, dimethylaminocarbonyloxopyrrolidinyl, dimethylmorpholinylcarbonyloxopyrrolidinyl, dioxopyrrolidinyloxopyrrolidinyl, ethyloxopyrrolidinyl, fluoropyrimidinylaminooxopyrrolidinyl, fluoropyrimidinyloxyoxopyrrolidinyl, hydroxyoxopyrrolidinyl, hydroxyazetidinylcarbonyloxopyrrolidinyl,

hydroxyethyl(methyl)aminocarbonyloxopyrrolidinyl, hydroxy(dimethyl)oxopyrrolidinyl, hydroxydimethylethylaminooxopyrrolidinyl, hydroxymethyloxopyrrolidinyl, hydroxy(methyl)cyanooxopyrrolidinyl, hydroxymethyl(cyano)oxopyrrolidinyl, hydroxymethylethyloxopyrrolidinyl, hydroxypyrrolidinylcarbonyloxopyrrolidinyl, methoxyoxopyrrolidinyl, methoxymethyloxopyrrolidinyl, methyloxopyrrolidinyl, methyl(methylsulfonyl)aminooxopyrrolidinyl, methylaminocarbonyloxopyrrolidinyl, methylcyanooxopyrrolidinyl, methyl(hydroxymethyl)oxopyrrolidinyl, methylmorpholinylcarbonyloxopyrrolidinyl, methyloxadiazolyloxopyrrolidinyl, methyloxadiazolyl(methyl)oxopyrrolidinyl, methyloxazolyloxopyrrolidinyl, methylpyrazolyloxopyrrolidinyl, methylsulfonyloxopyrrolidinyl, methylsulfonylaminooxopyrrolidinyl, methylsulfonylmethyloxopyrrolidinyl, morpholinylcarbonyloxopyrrolidinyl, morpholinylcarbonyl(methyl)oxopyrrolidinyl, oxadiazolyloxopyrrolidinyl, oxadiazolyl(methyl)oxopyrrolidinyl, oxazolyloxopyrrolidinyl, oxazolylaminocarbonyloxopyrrolidinyl, oxazolylcarbonyl(methyl)aminooxopyrrolidinyl, oxazolyl(methyl)aminocarbonyloxopyrrolidinyl, oxomorpholinyloxopyrrolidinyl, oxooxazolidinyloxopyrrolidinyl, oxopyrrolidinyloxopyrrolidinyl, phenyloxopyrrolidinyl, phenyl(hydroxy)oxopyrrolidinyl, pyrazolylmethyloxopyrrolidinyl, pyridinyloxopyrrolidinyl, pyrimidinyloxopyrrolidinyl, pyrimidinylaminooxopyrrolidinyl, pyrimidinyl(methyl)aminooxopyrrolidinyl, pyrimidinyloxyoxopyrrolidinyl, pyrimidinyloxy(hydroxy)oxopyrrolidinyl, pyrimidinyloxy(hydroxy)(methyl)oxopyrrolidinyl, pyrimidinyloxymethyloxopyrrolidinyl, pyrrolidinylcarbonyloxopyrrolidinyl, thiazolyloxopyrrolidinyl, trifluoromethyloxopyrrolidinyl, trifluoromethyloxadiazolyloxopyrrolidinyl, oxotetrahydrofuro[3,4-c]pyrrolyl, oxotetrahydroimidazo[5,1-c][1,4]oxazinyl, oxopyrrolo[3,4-b]pyridinyl or oxopyrrolo[3,2-c]pyridinyl;

R^2 and R^3 are independently selected from hydrogen and methyl with the proviso that R^2 is not methyl when R^3 is H;

R^4 is chloropyridinyl, difluoromethylpyridinyl, fluorochloropyridinyl, fluorodifluoromethylpyridinyl, trifluoromethylpyridinyl, difluorochlorophenyl,

difluorodifluoromethylphenyl, fluorochlorophenyl, fluorotrifluoromethylphenyl, trifluorophenyl;

Y is CH;

Q is N;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

16. A compound of formula (I) according to claim 14 or 15, wherein R^1 is

oxoazabicyclo[3.1.0]hexanyl;

oxodiazaspiro[3.4]octanyl substituted by C_{1-6}alkoxycarbonyl or pyrimidinyl;

oxoimidazolidinyl;

oxoindolinyl;

oxomorpholinyl, said oxomorpholinyl being unsubstituted or substituted once or twice by C_{1-6}alkyl;

oxooxaazaspiro[2.4]heptanyl;

oxooxaazaspiro[4.5]decanyl;

oxooxazinanyl, said oxooxazinanyl being unsubstituted or substituted once or twice by C_{1-6}alkyl;

oxooxazolidinyl, said oxooxazolidinyl being unsubstituted or substituted twice by C_{1-6}alkyl;

oxopyrrolidinyl said oxopyrrolidinyl being unsubstituted or substituted with one or two substituents independently selected from $(C_{1-6}alkyl)_2$aminocarbonyl, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkyloxadiazolyl, cyano, halopyrimidinyloxy, haloC_{1-6}alkyl, hydroxy, hydroxyC_{1-6}alkyl, morpholinylcarbonyl, oxadiazolyl, pyrimidinylamino, pyrimidinyloxy and pyrrolidinylcarbonyl;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

17. A compound of formula (I) according to any one of claims 14 to 16, wherein R^1 is oxoazabicyclo[3.1.0]hexanyl, methoxycarbonyloxodiazaspiro[3.4]octanyl, ethoxycarbonyloxodiazaspiro[3.4]octanyl, pyrimidinyloxodiazaspiro[3.4]octanyl, oxoimidazolidinyl, oxoindolinyl, oxomorpholinyl, dimethyloxomorpholinyl, oxooxaazaspiro[4.5]decanyl, oxooxaazaspiro[2.4]heptanyl, oxooxazinanyl, methyloxooxazinanyl, dimethyloxooxazinanyl, oxooxazolidinyl, dimethyloxooxazolidinyl, oxopyrrolidinyl, cyanooxopyrrolidinyl, hydroxyoxopyrrolidinyl, methoxyoxopyrrolidinyl, trifluoromethyloxopyrrolidinyl, pyrimidinylaminooxopyrrolidinyl, oxadiazolyloxopyrrolidinyl,

methyloxadiazolyloxopyrrolidinyl, hydroxymethylcyanooxopyrrolidinyl, methylcyanooxopyrrolidinyl, methyl(hydroxymethyl)oxopyrrolidinyl, morpholinylcarbonyloxopyrrolidinyl, pyrimidinyloxyoxopyrrolidinyl, pyrimidinyloxy(hydroxy)oxopyrrolidinyl, fluoropyrimidinyloxyoxopyrrolidinyl, dimethylaminocarbonyloxopyrrolidinyl or pyrrolidinylcarbonyloxopyrrolidinyl; or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

18. A compound of formula (I) according to any one of claims 14 to 17, wherein R^4 is pyridinyl substituted by haloC_{1-6}alkyl; or phenyl substituted with two or three substituents independently selected from halogen and haloC_{1-6}alkyl; or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

19. A compound of formula (I) according to any one of claims 14 to 18, wherein R^4 is difluoromethylpyridinyl, fluorochlorophenyl, difluorodifluoromethylphenyl or trifluorophenyl; or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

20. A compound of formula (I) according to any one of claims 14 to 19, wherein

R^1 is oxoazabicyclo[3.1.0]hexanyl;

oxodiazaspiro[3.4]octanyl substituted with C_{1-6}alkoxycarbonyl or pyrimidinyl;

oxoimidazolidinyl;

oxoindolinyl;

oxomorpholinyl, said oxomorpholinyl being unsubstituted or substituted once or twice by C_{1-6}alkyl;

oxooxaazaspiro[2.4]heptanyl;

oxooxaazaspiro[4.5]decanyl;

oxooxazinanyl, said oxooxazinanyl being unsubstituted or substituted once ro twice by C_{1-6}alkyl;

oxooxazolidinyl, said oxooxazolidinyl being unsubstituted or substituted once or twice by C_{1-6}alkyl;

oxopyrrolidinyl said oxopyrrolidinyl being unsubstituted or substituted with one or two substituents independently selected from $(C_{1-6}alkyl)_2$aminocarbonyl, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkyloxadiazolyl, cyano, halopyrimidinyloxy, haloC_{1-}

$_{6}$alkyl, hydroxy, hydroxyC_{1-6}alkyl, morpholinylcarbonyl, oxadiazolyl, pyrimidinylamino, pyrimidinyloxy and pyrrolidinylcarbonyl;

R^2 is H;

R^3 is H or C_{1-6}alkyl;

R^4 is pyridinyl substituted by haloC_{1-6}alkyl; or

phenyl substituted with two or three substituents independently selected from halogen and haloC_{1-6}alkyl;

Y is CH;

Q is N;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

21. A compound of formula (I) according to any one of claims 14 to 20, wherein

R^1 is oxoazabicyclo[3.1.0]hexanyl, methoxycarbonyloxodiazaspiro[3.4]octanyl, ethoxycarbonyloxodiazaspiro[3.4]octanyl, pyrimidinyloxodiazaspiro[3.4]octanyl, oxoimidazolidinyl, oxoindolinyl, oxomorpholinyl, dimethyloxomorpholinyl, oxooxaazaspiro[4.5]decanyl, oxooxaazaspiro[2.4]heptanyl, oxooxazinanyl, methyloxooxazinanyl, dimethyloxooxazinanyl, oxooxazolidinyl, dimethyloxooxazolidinyl, oxopyrrolidinyl, cyanooxopyrrolidinyl, hydroxyoxopyrrolidinyl, methoxyoxopyrrolidinyl, trifluoromethyloxopyrrolidinyl, pyrimidinylaminooxopyrrolidinyl, oxadiazolyloxopyrrolidinyl, methyloxadiazolyloxopyrrolidinyl, hydroxymethylcyanooxopyrrolidinyl, methylcyanooxopyrrolidinyl, methyl(hydroxymethyl)oxopyrrolidinyl, morpholinylcarbonyloxopyrrolidinyl, pyrimidinyloxyoxopyrrolidinyl, pyrimidinyloxy(hydroxy)oxopyrrolidinyl, fluoropyrimidinyloxyoxopyrrolidinyl, dimethylaminocarbonyloxopyrrolidinyl or pyrrolidinylcarbonyloxopyrrolidinyl;

R^2 is H;

R^3 is H or methyl;

R^4 is difluoromethylpyridinyl, fluorochlorophenyl, difluorodifluoromethylphenyl or trifluorophenyl;

Y is CH;

Q is N;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

22. A compound according to claim 20 or 21, selected from

N-(3-chloro-4-fluoro-phenyl)-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

6-methyl-3-(2-oxopyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-cyano-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-hydroxy-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(3-oxomorpholin-4-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(2-oxooxazolidin-3-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-methoxy-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(4-cyano-2-oxo-pyrrolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4R)-4-cyano-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4S)-4-cyano-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-6-methyl-3-[2-oxo-4-(trifluoromethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(5,5-dimethyl-2-oxo-oxazolidin-3-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxo-3-azabicyclo[3.1.0]hexan-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(pyrimidin-2-ylamino)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-6-methyl-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-3-(5,5-dimethyl-2-oxo-oxazolidin-3-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-3-(5,5-dimethyl-2-oxo-oxazolidin-3-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(5-methyl-2-oxo-1,3-oxazinan-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(1,3,4-oxadiazol-2-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(5-methyl-1,3,4-oxadiazol-2-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(3-methyl-1,2,4-oxadiazol-5-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(5-methyl-1,2,4-oxadiazol-3-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxo-1,3-oxazinan-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(5,5-dimethyl-2-oxo-1,3-oxazinan-3-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(3-oxo-8-oxa-2-azaspiro[4.5]decan-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(5-oxo-4-oxa-6-azaspiro[2.4]heptan-6-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

methyl 6-[(6S)-6-methyl-5-[(3,4,5-trifluorophenyl)carbamoyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-7-oxo-2,6-diazaspiro[3.4]octane-2-carboxylate;

ethyl 6-[(6S)-6-methyl-5-[(3,4,5-trifluorophenyl)carbamoyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-7-oxo-2,6-diazaspiro[3.4]octane-2-carboxylate;

(6S)-6-methyl-3-(7-oxo-2-pyrimidin-2-yl-2,6-diazaspiro[3.4]octan-6-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxoindolin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxopyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-cyano-4-(hydroxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(4-cyano-4-methyl-2-oxo-pyrrolidin-1-yl)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(hydroxymethyl)-4-methyl-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(2,2-dimethyl-5-oxo-morpholin-4-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-6-methyl-3-(2-oxoimidazolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4S)-4-methoxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4R)-4-methoxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[(4S)-2-oxo-4-pyrimidin-2-yloxy-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4S)-4-(5-fluoropyrimidin-2-yl)oxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(dimethylcarbamoyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(pyrrolidine-1-carbonyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[(4R)-2-oxo-4-pyrimidin-2-yloxy-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(3-cyano-2-methyl-5-oxo-pyrrolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(5-hydroxy-2-oxo-1,3-oxazinan-3-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide; and

(6S)-3-[(3S,4R)-3-hydroxy-2-oxo-4-pyrimidin-2-yloxy-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

23. A compound of formula (I) according to claim 1 or 2, wherein

R^1 is oxopyrrolidinyl, said oxopyrrolidinyl being unsubstituted or substituted with one or two substituents independently selected from $(C_{1-6}alkyl)_2$aminocarbonyl, $(C_{1-6}alkyl)_2$morpholinylcarbonyl, C_{1-6}alkoxy, C_{1-6}alkoxyC_{1-6}alkyl, C_{1-6}alkyl, C_{1-6}alkyl(C_{1-6}alkylsulfonyl)amino, C_{1-6}alkylaminocarbonyl, C_{1-6}alkylcarbonylamino, C_{1-6}alkylmorpholinylcarbonyl, C_{1-6}alkyloxadiazolyl, C_{1-6}alkyloxazolyl, C_{1-6}alkylpyrazolyl, C_{1-6}alkylsulfonyl, C_{1-6}alkylsulfonylamino, C_{1-6}alkylsulfonylC_{1-6}alkyl, cyano, dioxopyrrolidinyl, haloC_{1-6}alkyl, haloC_{1-6}alkyloxadiazolyl, halopiperidinylcarbonyl, halopyrimidinylamino, halopyrimidinyloxy, halopyrrolidinylcarbonyl, hydroxy, hydroxyazetidinylcarbonyl, hydroxyC_{1-6}alkyl, hydroxyC_{1-6}alkyl(C_{1-6}alkyl)aminocarbonyl, hydroxyC_{1-6}alkylaminocarbonyl, hydroxypyrrolidinylcarbonyl, morpholinylcarbonyl, oxadiazolyl, oxazolyl, oxazolylaminocarbonyl, oxazolyl(C_{1-6}alkyl)aminocarbonyl, oxazolylcarbonyl(C_{1-6}alkyl)amino, oxomorpholinyl, oxooxazolidinyl, oxopyrrolidinyl, phenyl, pyrazolylC_{1-6}alkyl, pyridinyl, pyrimidinyl, pyrimidinylamino, pyrimidinyl(C_{1-6}alkyl)amino, pyrimidinyloxy, pyrimidinyloxyC_{1-6}alkyl, pyrrolidinylcarbonyl and thiazolyl;

R^2 and R^3 are independently selected from hydrogen and C_{1-6}alkyl with the proviso that R^2 is not C_{1-6}alkyl when R^3 is H;

R^4 is pyridinyl substituted with one or two substituents independently selected from halogen and haloC_{1-6}alkyl;

phenyl substituted with one, two or three substituents independently selected from halogen and haloC_{1-6}alkyl;

Y is CH;

Q is N;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

24. A compound of formula (I) according to claim 23, wherein

R^1 is oxopyrrolidinyl, acetylaminooxopyrrolidinyl, cyanooxopyrrolidinyl, difluoropiperidinylcarbonyl(methyl)oxopyrrolidinyl, difluoropyrrolidinylcarbonyloxopyrrolidinyl, difluoropyrrolidinylcarbonyl(methyl)oxopyrrolidinyl, dihydroxyoxopyrrolidinyl, dimethyloxopyrrolidinyl, dimethylaminocarbonyloxopyrrolidinyl, dimethylmorpholinylcarbonyloxopyrrolidinyl, dioxopyrrolidinyloxopyrrolidinyl, ethyloxopyrrolidinyl, fluoropyrimidinylaminooxopyrrolidinyl, fluoropyrimidinyloxyoxopyrrolidinyl, hydroxyoxopyrrolidinyl, hydroxyazetidinylcarbonyloxopyrrolidinyl, hydroxyethyl(methyl)aminocarbonyloxopyrrolidinyl, hydroxy(dimethyl)oxopyrrolidinyl, hydroxydimethylethylaminooxopyrrolidinyl, hydroxymethyloxopyrrolidinyl, hydroxy(methyl)cyanooxopyrrolidinyl, hydroxymethyl(cyano)oxopyrrolidinyl, hydroxymethylethyloxopyrrolidinyl, hydroxypyrrolidinylcarbonyloxopyrrolidinyl, methoxyoxopyrrolidinyl, methoxymethyloxopyrrolidinyl, methyloxopyrrolidinyl, methyl(methylsulfonyl)aminooxopyrrolidinyl, methylaminocarbonyloxopyrrolidinyl, methylcyanooxopyrrolidinyl, methyl(hydroxymethyl)oxopyrrolidinyl, methylmorpholinylcarbonyloxopyrrolidinyl, methyloxadiazolyloxopyrrolidinyl, methyloxadiazolyl(methyl)oxopyrrolidinyl, methyloxazolyloxopyrrolidinyl, methylpyrazolyloxopyrrolidinyl, methylsulfonyloxopyrrolidinyl, methylsulfonylaminooxopyrrolidinyl, methylsulfonylmethyloxopyrrolidinyl, morpholinylcarbonyloxopyrrolidinyl, morpholinylcarbonyl(methyl)oxopyrrolidinyl, oxadiazolyloxopyrrolidinyl, oxadiazolyl(methyl)oxopyrrolidinyl, oxazolyloxopyrrolidinyl, oxazolylaminocarbonyloxopyrrolidinyl, oxazolylcarbonyl(methyl)aminooxopyrrolidinyl, oxazolyl(methyl)aminocarbonyloxopyrrolidinyl, oxomorpholinyloxopyrrolidinyl, oxooxazolidinyloxopyrrolidinyl, oxopyrrolidinyloxopyrrolidinyl, phenyloxopyrrolidinyl, phenyl(hydroxy)oxopyrrolidinyl, pyrazolylmethyloxopyrrolidinyl, pyridinyloxopyrrolidinyl,

pyrimidinyloxopyrrolidinyl, pyrimidinylaminooxopyrrolidinyl, pyrimidinyl(methyl)aminooxopyrrolidinyl, pyrimidinyloxyoxopyrrolidinyl, pyrimidinyloxy(hydroxy)oxopyrrolidinyl, pyrimidinyloxy(hydroxy)(methyl)oxopyrrolidinyl, pyrimidinyloxymethyloxopyrrolidinyl, pyrrolidinylcarbonyloxopyrrolidinyl, thiazolyloxopyrrolidinyl, trifluoromethyloxopyrrolidinyl or trifluoromethyloxadiazolyloxopyrrolidinyl;

R^2 and R^3 are independently selected from hydrogen and methyl with the proviso that R^2 is not methyl when R^3 is H;

R^4 is chloropyridinyl, difluoromethylpyridinyl, fluorochloropyridinyl, trifluoromethylpyridinyl, difluorochlorophenyl, difluorodifluoromethylphenyl, fluorochlorophenyl, fluorotrifluoromethylphenyl or trifluorophenyl;

Y is CH;

Q is N;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

25. A compound of formula (I) according to claim 23 or 24, wherein R^1 is oxopyrrolidinyl, said oxopyrrolidinyl being unsubstituted or substituted with one or two substituents independently selected from $(C_{1-6}alkyl)_2$aminocarbonyl, C_{1-6}alkoxy, C_{1-6}alkyl, C_{1-6}alkyloxadiazolyl, cyano, haloC_{1-6}alkyl, halopyrimidinyloxy, hydroxy, hydroxyC_{1-6}alkyl, morpholinylcarbonyl, oxadiazolyl, pyrimidinylamino, pyrimidinyloxy and pyrrolidinylcarbonyl; or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

26. A compound of formula (I) according to any one of claims 23 to 25, wherein R^1 is oxopyrrolidinyl, cyanooxopyrrolidinyl, hydroxyoxopyrrolidinyl, methoxyoxopyrrolidinyl, trifluoromethyloxopyrrolidinyl, pyrimidinylaminooxopyrrolidinyl, oxadiazolyloxopyrrolidinyl, methyloxadiazolyloxopyrrolidinyl, hydroxymethylcyanooxopyrrolidinyl, methylcyanooxopyrrolidinyl, methyl(hydroxymethyl)oxopyrrolidinyl, pyrimidinyloxyoxopyrrolidinyl, pyrimidinyloxy(hydroxy)oxopyrrolidinyl, fluoropyrimidinyloxyoxopyrrolidinyl, morpholinylcarbonyloxopyrrolidinyl, dimethylaminocarbonyloxopyrrolidinyl or pyrrolidinylcarbonyloxopyrrolidinyl; or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

27. A compound of formula (I) according to any one of claims 23 to 26, wherein R^2 is H; R^3 is H or C_{1-6}alkyl; or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

28. A compound of formula (I) according to any one of claims 23 to 27, wherein R^2 is H; R^3 is H or methyl; or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

29. A compound of formula (I) according to any one of claims 23 to 28, wherein R^4 is pyridinyl substituted by haloC_{1-6}alkyl; or phenyl substituted with one, two or three substituents independently selected from halogen and haloC_{1-6}alkyl; or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

30. A compound of formula (I) according to any one of claims 23 to 29, wherein R^4 is difluoromethylpyridinyl, fluorochlorophenyl, difluorodifluoromethylphenyl or trifluorophenyl; or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

31. A compound of formula (I) according to any one of claims 23 to 30, wherein

R^1 is oxopyrrolidinyl, said oxopyrrolidinyl being unsubstituted or substituted with one or two substituents independently selected from $(C_{1-6}alkyl)_2$aminocarbonyl, C_{1-6}alkoxy, C_{1-6}alkyl, C_{1-6}alkyloxadiazolyl, cyano, haloC_{1-6}alkyl, halopyrimidinyloxy, hydroxy, hydroxyC_{1-6}alkyl, morpholinylcarbonyl, oxadiazolyl, pyrimidinylamino, pyrimidinyloxy and pyrrolidinylcarbonyl;

R^2 is H;

R^3 is H or C_{1-6}alkyl;

R^4 is pyridinyl substituted by haloC_{1-6}alkyl; or

phenyl substituted with one, two or three substituents independently selected from halogen and haloC_{1-6}alkyl;

Y is CH;

Q is N;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

32. A compound of formula (I) according to any one of claims 23 to 31, wherein

R^1 is oxopyrrolidinyl, cyanooxopyrrolidinyl, hydroxyoxopyrrolidinyl, methoxyoxopyrrolidinyl, trifluoromethyloxopyrrolidinyl,

pyrimidinylaminooxopyrrolidinyl, oxadiazolyloxopyrrolidinyl, methyloxadiazolyloxopyrrolidinyl, hydroxymethylcyanooxopyrrolidinyl, methylcyanooxopyrrolidinyl, methyl(hydroxymethyl)oxopyrrolidinyl, pyrimidinyloxyoxopyrrolidinyl, pyrimidinyloxy(hydroxy)oxopyrrolidinyl, fluoropyrimidinyloxyoxopyrrolidinyl, morpholinylcarbonyloxopyrrolidinyl, dimethylaminocarbonyloxopyrrolidinyl or pyrrolidinylcarbonyloxopyrrolidinyl;

R^2 is H;

R^3 is H or C_{1-6}alkyl;

R^4 is difluoromethylpyridinyl, fluorochlorophenyl, difluorodifluoromethylphenyl or trifluorophenyl;

Y is CH;

Q is N;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

33. A compound according to any one of claims 23 to 32, selected from

N-(3-chloro-4-fluoro-phenyl)-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

6-methyl-3-(2-oxopyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-cyano-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-hydroxy-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-methoxy-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(4-cyano-2-oxo-pyrrolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4R)-4-cyano-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4S)-4-cyano-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-6-methyl-3-[2-oxo-4-(trifluoromethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(pyrimidin-2-ylamino)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(1,3,4-oxadiazol-2-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(5-methyl-1,3,4-oxadiazol-2-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(3-methyl-1,2,4-oxadiazol-5-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(5-methyl-1,2,4-oxadiazol-3-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxopyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-cyano-4-(hydroxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(4-cyano-4-methyl-2-oxo-pyrrolidin-1-yl)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(hydroxymethyl)-4-methyl-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4S)-4-methoxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4R)-4-methoxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[(4S)-2-oxo-4-pyrimidin-2-yloxy-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4S)-4-(5-fluoropyrimidin-2-yl)oxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(morpholine-4-carbonyl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(dimethylcarbamoyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(pyrrolidine-1-carbonyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[(4R)-2-oxo-4-pyrimidin-2-yloxy-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(3-cyano-2-methyl-5-oxo-pyrrolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide; and

(6S)-3-[(3S,4R)-3-hydroxy-2-oxo-4-pyrimidin-2-yloxy-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

34. A compound according to any one of claims 1 or 2, selected from

3-(4-fluorophenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N,3-diphenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(3-fluorophenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(3-chlorophenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-phenyl-3-[3-(trifluoromethyl)phenyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2-fluorophenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2-chlorophenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-phenyl-3-[2-(trifluoromethyl)phenyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

1-(4-fluorophenyl)-N-phenyl-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

3-(4-fluorophenyl)-N-phenyl-6,7-dihydro-4H-triazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluorophenyl)-N-[3-(trifluoromethyl)phenyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-8-(4-fluorophenyl)-3,4-dihydro-1H-pyrrolo[1,2-a]pyrazine-2-carboxamide;

N-(2-fluorophenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N,3-bis(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
N-(3-chlorophenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
N-(3-cyanophenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
N-(4-chlorophenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
3-(2-cyanophenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
N-(3-fluorophenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
N-(4-chloro-3-fluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
N-(3-chloro-4-fluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
3-(4-fluorophenyl)-N-(4-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
N-(4-cyanophenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
N-(3-chloro-4-fluoro-phenyl)-3-(2-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
3-(3-methoxyphenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
3-cyclopentyl-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
3-(2-methoxyphenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
N-phenyl-3-[4-(trifluoromethyl)-2-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
3-(4-cyano-2-pyridyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
N-(3-chlorophenyl)-3-(2-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
N-(3-chlorophenyl)-3-(o-tolyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
N-(5-fluoro-6-methyl-2-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;
3-(2-fluorophenyl)-N-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2-fluorophenyl)-N-[4-fluoro-3-(trifluoromethyl)phenyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chlorophenyl)-3-(2,4-difluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chlorophenyl)-3-(2,3-difluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(3-cyano-2-pyridyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(3-chloro-2-fluoro-phenyl)-N-(3-chlorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(5-chloro-2-fluoro-phenyl)-N-(3-chlorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chlorophenyl)-3-(2,5-difluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-[3-(difluoromethyl)phenyl]-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(5-fluoro-6-methyl-2-pyridyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(5-fluoro-4-methyl-2-pyridyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-phenyl-3-(2-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide+H31;

N-phenyl-3-thiazol-2-yl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-phenyl-3-[4-(trifluoromethyl)thiazol-2-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(5-chlorothiazol-2-yl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(3,4-difluorophenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(6-chloro-2-pyridyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(2,4-difluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2,4-difluorophenyl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluoro-3-methyl-phenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluorophenyl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-[(3-chloro-4-fluoro-phenyl)methyl]-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-[(3,5-dichlorophenyl)methyl]-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(4-chloro-5-methyl-2-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-chloro-2-pyridyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-[(2-chloro-3-fluoro-phenyl)methyl]-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-[(2,6-dichlorophenyl)methyl]-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2,4-difluorophenyl)-N-(5-fluoro-6-methyl-2-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(4-fluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluorophenyl)-N-(2-methyl-1,3-benzothiazol-5-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(benzothiophen-3-yl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2,4-difluorophenyl)-N-[2-(trifluoromethyl)-4-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(3-cyclopropylphenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2-hydroxyphenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-[4-(trifluoromethyl)-2-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(5-fluoro-4-methyl-2-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(5-fluoro-2-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2-chloro-4-pyridyl)-3-(2,4-difluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-[4-(trifluoromethyl)-2-pyridyl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N,3-bis(3-chloro-4-fluoro-phenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-cyclohexyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyano-4-fluoro-phenyl)-3-(5-fluoro-4-methyl-2-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(5-fluoro-2-pyridyl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyano-4-fluoro-phenyl)-3-(5-fluoro-2-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluorophenyl)-N-(1H-indol-6-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-cyclopentyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyano-4-fluoro-phenyl)-3-cyclopentyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluorophenyl)-N-[4-fluoro-3-(trifluoromethyl)phenyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(4-fluoro-3-methyl-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-cyclopentyl-N-indan-5-yl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-cyclopentyl-N-indan-1-yl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-benzyl-3-cyclopentyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyano-4-fluoro-phenyl)-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyano-4-fluoro-phenyl)-3-(4-fluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-pyrrolidin-1-yl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2,4-difluorophenyl)-6-methyl-N-[2-(trifluoromethyl)-4-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(1-piperidyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(4,4-difluoro-1-piperidyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-thiazol-2-yl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2-chloro-4-pyridyl)-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(5-fluoro-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(3,3-difluoro-1-piperidyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2-chloro-4-pyridyl)-3-cyclopentyl-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2-cyano-4-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2-chloro-6-methoxy-4-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(5-fluoro-2-pyridyl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyano-4-fluoro-phenyl)-3-(5-fluoro-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6R)-N-(3-chloro-4-fluoro-phenyl)-3-(4-fluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-fluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2-chloro-4-pyridyl)-3-cyclopentyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(benzofuran-6-yl)-3-cyclopentyl-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyano-4-fluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyano-5-fluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluorophenyl)-N-[4-methyl-3-(trifluoromethyl)phenyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-[3-chloro-5-(trifluoromethyl)phenyl]-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3,4-difluorophenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-cyano-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluorophenyl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3,5-difluorophenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-[4-chloro-3-(trifluoromethyl)phenyl]-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-ethylphenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-ethynylphenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluorophenyl)-N-(3-isopropylphenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluorophenyl)-N-(3-methoxyphenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-phenyl-3-[2-(trifluoromethoxy)phenyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(3-chloro-4-fluoro-phenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(m-tolyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(3-bromophenyl)-N-phenyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-ethynyl-4-fluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-5-fluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2-chloro-4-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2,6-dimethyl-4-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluorophenyl)-N-[2-(trifluoromethyl)-4-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-1-(4-fluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

N-(3-bromo-4-fluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-[3-(difluoromethoxy)phenyl]-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluorophenyl)-N-[4-fluoro-3-(trifluoromethoxy)phenyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-[3-(difluoromethyl)phenyl]-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluorophenyl)-N-(m-tolyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-phenyl-3-[3-(trifluoromethoxy)phenyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

1-(2,4-difluorophenyl)-N-(3-ethynyl-4-fluoro-phenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-1-(2,4-difluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

N-(3-cyano-4-fluoro-phenyl)-1-(2,4-difluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

N-(3-cyano-4,5-difluoro-phenyl)-1-(2,4-difluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

1-(2,4-difluorophenyl)-N-(3,4,5-trifluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

3-(2,4-difluorophenyl)-N-(3-ethynyl-4-fluoro-phenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(6-chloro-5-fluoro-2-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyclopropylphenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyano-4-fluoro-phenyl)-3-(2,4-difluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(6-chloro-5-fluoro-2-pyridyl)-3-(2,4-difluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3,4-difluoro-5-methyl-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4,5-difluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyclopropyl-4,5-difluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-[3-(1,1-difluoroethyl)phenyl]-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(4-chloro-5-fluoro-2-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(2-chloro-5-fluoro-4-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyclopropyl-4-fluoro-phenyl)-3-(2,4-difluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2-chloro-4-pyridyl)-1-(2,4-difluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

1-(2,4-difluorophenyl)-N-[2-(trifluoromethyl)-4-pyridyl]-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-triazolo[1,5-a]pyrazine-5-carboxamide;

N-(6-chloro-5-fluoro-2-pyridyl)-1-(2,4-difluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(2,4-difluorophenyl)-6,7-dihydro-4H-triazolo[1,5-a]pyrazine-5-carboxamide;

N-(3,4-difluoro-5-methyl-phenyl)-3-(5-fluoro-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyclopropyl-4-fluoro-phenyl)-3-(5-fluoro-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4,5-difluoro-phenyl)-3-(5-fluoro-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3,4-difluoro-5-methoxy-phenyl)-3-(5-fluoro-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-cyclopropyl-4,5-difluoro-phenyl)-3-(5-fluoro-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(6-chloro-5-fluoro-2-pyridyl)-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-1-cyclopentyl-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

1-cyclopentyl-N-(3,4,5-trifluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

1-cyclopentyl-N-(3,4-difluoro-5-methyl-phenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

N-(3-cyclopropyl-4,5-difluoro-phenyl)-1-(2,4-difluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

N-(3,4-difluoro-5-methoxy-phenyl)-1-(2,4-difluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

N-(3,4-difluoro-5-methyl-phenyl)-1-(2,4-difluorophenyl)-6,8-dihydro-5H-imidazo[1,5-a]pyrazine-7-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(2-methylpyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-morpholino-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(4-methylpyrazol-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-benzyl-3-(4-fluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluorophenyl)-N-(2-fluoro-4-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2,4-difluorophenyl)-N-(2-fluoro-4-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(1,3-benzoxazol-6-yl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(4-fluorophenyl)-N-(2-methyl-4-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2,6-difluoro-4-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2,4-difluorophenyl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2,4-difluorophenyl)-N-(5-fluoro-4-methyl-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-cyclopentyl-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-cyclohexyl-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-tetrahydrofuran-3-yl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

6-methyl-3-(2-oxopyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(4-bicyclo[4.2.0]octa-1(6),2,4-trienyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(5-fluoropyrimidin-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(5-fluoro-4-methyl-pyrimidin-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2,4-difluorophenyl)-6-methyl-N-(2-methyl-4-pyridyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2-chloro-4-pyridyl)-3-(5-fluoro-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(4-methylpyrazol-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2-chloro-4-pyridyl)-6-methyl-3-[4-(trifluoromethyl)-2-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2-chloro-4-pyridyl)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2-bromo-4-pyridyl)-3-(4-fluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-2-methyl-4-pyridyl)-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2,4-difluorophenyl)-N-(5-fluoro-2-methyl-4-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(5-chloro-2-methyl-4-pyridyl)-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-[(2-chloro-3-fluoro-phenyl)methyl]-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2,4-difluorophenyl)-N-(5-fluoro-6-methyl-2-pyridyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(5-fluoro-2-pyridyl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(4-methylpyrazol-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(4-cyanopyrazol-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(4-fluoropyrazol-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-[4-fluoro-3-(trifluoromethyl)phenyl]-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-cyclopentyl-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-cyclopentyl-6-methyl-N-[2-(trifluoromethyl)-4-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(6-chloro-5-fluoro-2-pyridyl)-3-cyclopentyl-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(2-cyclopropyl-4-pyridyl)-3-(2,4-difluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(2,4-difluorophenyl)-N-[2-(dimethylamino)-4-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-[2-(methoxymethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-[3-(methoxymethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(3-methoxypyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(4,4-dimethyl-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-[3-(trifluoromethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(3-cyanopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(3-azabicyclo[3.1.0]hexan-3-yl)-N-(3-chloro-4-fluoro-phenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(3-hydroxy-3-methyl-pyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(2,2-dimethylmorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-[2-(difluoromethyl)-4-pyridyl]-3-(2,4-difluorophenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(3-methyl-5-oxo-morpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(3,3-difluoropyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-[trans-2,6-dimethylmorpholin-4-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-[cis-2,6-dimethylmorpholin-4-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-hydroxy-1-piperidyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(3-methyl-2-oxo-imidazolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-cyano-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(4-fluorophenyl)-7-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4,5-difluoro-phenyl)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-hydroxy-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(3-oxomorpholin-4-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

3-(1-acetyl-4-piperidyl)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4,5-difluoro-phenyl)-6-methyl-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-[4-(methylcarbamoyl)-2-oxo-pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(2-oxooxazolidin-3-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-methoxy-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(4-cyano-2-oxo-pyrrolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4R)-4-cyano-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4S)-4-cyano-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-6-methyl-3-[2-oxo-4-(trifluoromethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(2-acetyl-7-oxo-2,6-diazaspiro[3.4]octan-6-yl)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-methyl-5-oxo-morpholin-4-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-(3-chloro-4-fluoro-phenyl)-3-(2,5-dioxopiperazin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4,4-dimethyl-2-oxo-imidazolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(3,6-dioxo-4,7,8,8a-tetrahydro-1H-pyrrolo[1,2-a]pyrazin-2-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(4-oxazol-5-yl-2-oxo-pyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(3-methylsulfonyl-5-oxo-imidazolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(5,5-dimethyl-2-oxo-oxazolidin-3-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S,7S)-6,7-dimethyl-3-(2-oxopyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(6-oxo-5-azaspiro[2.4]heptan-5-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxo-3-azabicyclo[3.1.0]hexan-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(4-methyl-2-oxo-pyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-[2-oxo-4-(trifluoromethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(3-hydroxy-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4,4-dimethyl-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-3-(4,4-dimethyl-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(trifluoromethyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(2-chloro-4-pyridyl)-6-methyl-3-[2-oxo-4-(trifluoromethyl)pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S,7R)-6,7-dimethyl-3-(2-oxopyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(3S)-3-hydroxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(6-chloro-5-fluoro-2-pyridyl)-3-(4,4-dimethyl-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(3R)-3-hydroxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[6-(difluoromethyl)-5-fluoro-2-pyridyl]-6-methyl-3-(3-oxo-2-azaspiro[4.4]nonan-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-6-methyl-3-(3-oxo-2-azaspiro[4.4]nonan-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(pyrimidin-2-yloxymethyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(pyrazol-1-ylmethyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(pyrimidin-2-ylamino)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-[(5-fluoropyrimidin-4-yl)amino]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-6-methyl-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-3-(5,5-dimethyl-2-oxo-oxazolidin-3-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S,7S)-6,7-dimethyl-3-(2-oxoimidazolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S,7S)-6,7-dimethyl-3-(3-oxomorpholin-4-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(3-benzoyl-5-oxo-imidazolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-3-(5,5-dimethyl-2-oxo-oxazolidin-3-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[6-(difluoromethyl)-5-fluoro-2-pyridyl]-3-(5,5-dimethyl-2-oxo-oxazolidin-3-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(5-methyl-2-oxo-1,3-oxazinan-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(2,4-dioxo-1H-pyrimidin-3-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(2,4-dioxopyrimidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(5-oxo-3-pyrimidin-2-yl-imidazolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(1,3,4-oxadiazol-2-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(5-methyl-1,3,4-oxadiazol-2-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(3-methyl-1,2,4-oxadiazol-5-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(5-methyl-1,2,4-oxadiazol-3-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-[5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl]pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-3-(5-fluoropyrimidin-2-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[5-(1-methylimidazol-2-yl)-2-oxo-oxazolidin-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxo-4-thiazol-5-yl-pyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxo-4-thiazol-2-yl-pyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxo-1,3-oxazinan-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxohexahydropyrimidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(5,5-dimethyl-2-oxo-1,3-oxazinan-3-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-[4-(methoxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(3-oxo-8-oxa-2-azaspiro[4.5]decan-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(3-methyl-2-oxo-pyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-[4-(hydroxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(methoxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(methoxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-[2-(trifluoromethyl)-4-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(4-oxo-3,3a,6,6a-tetrahydro-1H-furo[3,4-c]pyrrol-5-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-ethyl-2-oxo-pyrrolidin-1-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(8-oxo-2-oxa-7-azaspiro[4.4]nonan-7-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(4-methylsulfonyl-2-oxo-pyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(4-hydroxy-2-oxo-1-piperidyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(methylsulfonylmethyl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-[[methyl(methylsulfonyl)amino]methyl]-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxopyrrolidin-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxo-4-phenyl-pyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(1-hydroxy-1-methyl-ethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(4-acetamido-2-oxo-pyrrolidin-1-yl)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-[4-(methanesulfonamido)-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-[4-[methyl(methylsulfonyl)amino]-2-oxo-pyrrolidin-1-yl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(2,5-dioxopyrrolidin-1-yl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(2-oxopyrrolidin-1-yl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

N-methyl-N-[1-[(6S)-6-methyl-5-[(3,4,5-trifluorophenyl)carbamoyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-5-oxo-pyrrolidin-3-yl]oxazole-5-carboxamide;

N-methyl-N-[1-[(6S)-6-methyl-5-[(3,4,5-trifluorophenyl)carbamoyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-5-oxo-pyrrolidin-3-yl]oxazole-4-carboxamide;

N-methyl-N-[1-[(6S)-6-methyl-5-[(3,4,5-trifluorophenyl)carbamoyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-5-oxo-pyrrolidin-3-yl]oxazole-2-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(2-oxooxazolidin-3-yl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(3-oxomorpholin-4-yl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(5-methyl-2-oxo-oxazolidin-3-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(3-oxo-5,6,8,8a-tetrahydro-1H-imidazo[5,1-c][1,4]oxazin-2-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(3-oxo-5,6,8,8a-tetrahydro-1H-imidazo[5,1-c][1,4]oxazin-2-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(2-chloro-4-pyridyl)-3-(5,5-dimethyl-2-oxo-oxazolidin-3-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(5,5-dimethyl-2-oxo-oxazolidin-3-yl)-6-methyl-N-[2-(trifluoromethyl)-4-pyridyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(4-methyl-2-oxo-imidazolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[(4R)-2-oxo-4-phenyl-oxazolidin-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[(4S)-2-oxo-4-phenyl-oxazolidin-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxo-4-phenyl-imidazolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(4,4-dimethyl-2-oxo-imidazolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(5-oxo-4-oxa-6-azaspiro[2.4]heptan-6-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(6-oxo-5-oxa-7-azaspiro[3.4]octan-7-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

methyl 6-[(6S)-6-methyl-5-[(3,4,5-trifluorophenyl)carbamoyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-7-oxo-2,6-diazaspiro[3.4]octane-2-carboxylate;

ethyl 6-[(6S)-6-methyl-5-[(3,4,5-trifluorophenyl)carbamoyl]-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazin-3-yl]-7-oxo-2,6-diazaspiro[3.4]octane-2-carboxylate;

(6S)-6-methyl-3-(5-methyl-2-oxo-pyrrolidin-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-(oxazole-2-carbonyl)-7-oxo-2,6-diazaspiro[3.4]octan-6-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(7-oxo-2-pyrimidin-2-yl-2,6-diazaspiro[3.4]octan-6-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxoindolin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(1-oxoisoindolin-2-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(5-oxo-7H-pyrrolo[3,4-b]pyridin-6-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(5-fluoropyrimidin-2-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(hydroxymethyl)pyrazol-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(methoxymethyl)pyrazol-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxo-5-phenyl-oxazolidin-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-5-(2-pyridyl)oxazolidin-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-5-(4-pyridyl)oxazolidin-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-5-(3-pyridyl)oxazolidin-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(5-oxazol-4-yl-2-oxo-oxazolidin-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(2-methyloxazol-5-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(2-methyloxazol-4-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(3-pyridyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(4-oxazol-4-yl-2-oxo-pyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(2-pyridyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(4-pyridyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(2-oxopyrrolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxopyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(5-methyl-2-oxo-1-piperidyl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(4-cyano-2-oxo-pyrrolidin-1-yl)-N-[2-(difluoromethyl)-4-pyridyl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-cyano-4-(hydroxymethyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(4-cyano-4-methyl-2-oxo-pyrrolidin-1-yl)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(hydroxymethyl)-4-methyl-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-[methyl(pyrimidin-2-yl)amino]-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-6-methyl-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxooxazolidin-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-6-methyl-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(2-chloro-4-pyridyl)-6-methyl-3-(3-oxomorpholin-4-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxoimidazolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-(3-chloro-4-fluoro-phenyl)-3-(2,2-dimethyl-5-oxo-morpholin-4-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[(3S)-3-methyl-5-oxo-morpholin-4-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[3-(difluoromethyl)-4,5-difluoro-phenyl]-6-methyl-3-(2-oxoimidazolidin-1-yl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(3-acetyl-5-oxo-imidazolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-3-(2,2-dimethyl-5-oxo-morpholin-4-yl)-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4R)-4-hydroxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4S)-4-hydroxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4S)-4-methoxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4R)-4-methoxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-N-[2-(difluoromethyl)-4-pyridyl]-3-[(4S)-4-methoxy-2-oxo-pyrrolidin-1-yl]-6-methyl-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[(4S)-2-oxo-4-pyrimidin-2-yloxy-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(4S)-4-(5-fluoropyrimidin-2-yl)oxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-[2-hydroxyethyl(methyl)carbamoyl]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-[(2-hydroxy-1,1-dimethyl-ethyl)carbamoyl]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(morpholine-4-carbonyl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-[(3S)-3-hydroxypyrrolidine-1-carbonyl]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-[(3R)-3-hydroxypyrrolidine-1-carbonyl]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(3-hydroxyazetidine-1-carbonyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(dimethylcarbamoyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[2-oxo-4-(pyrrolidine-1-carbonyl)pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(oxazol-2-ylcarbamoyl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(2,2-dimethylmorpholine-4-carbonyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-[(2R)-2-methylmorpholine-4-carbonyl]-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-[(2S)-2-methylmorpholine-4-carbonyl]-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-[trans-2,6-dimethylmorpholine-4-carbonyl]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-[cis-2,6-dimethylmorpholine-4-carbonyl]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(3,3-difluoropyrrolidine-1-carbonyl)-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-[methyl(oxazol-2-yl)carbamoyl]-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(3,3-difluoropyrrolidine-1-carbonyl)-4-methyl-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-(4,4-difluoropiperidine-1-carbonyl)-4-methyl-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-methyl-4-(morpholine-4-carbonyl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-methyl-4-(5-methyl-1,3,4-oxadiazol-2-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-methyl-4-(1,3,4-oxadiazol-2-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-methyl-4-(3-methyl-1,2,4-oxadiazol-5-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-methyl-4-(5-methyl-1,2,4-oxadiazol-3-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[(2S)-2-oxazol-5-yl-5-oxo-morpholin-4-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[5-(3-methyl-1,2,4-oxadiazol-5-yl)-2-oxo-oxazolidin-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[5-(6-chloro-3-pyridyl)-2-oxo-oxazolidin-3-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[5-(5-fluoro-2-pyridyl)-2-oxo-oxazolidin-3-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[5-(6-fluoro-2-pyridyl)-2-oxo-oxazolidin-3-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[4-(1-methylpyrazol-4-yl)-2-oxo-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxo-4-pyrimidin-5-yl-pyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[4-[(5-fluoropyrimidin-2-yl)amino]-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[(4R)-2-oxo-4-pyrimidin-2-yloxy-pyrrolidin-1-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(3R,4R)-3,4-dihydroxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(3-hydroxy-4,4-dimethyl-2-oxo-pyrrolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxo-3H-pyrrolo[3,2-c]pyridin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(6-oxo-4,7-dihydropyrazolo[1,5-a]pyrazin-5-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(3-cyano-2-methyl-5-oxo-pyrrolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(5-hydroxy-2-oxo-1,3-oxazinan-3-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(7-oxo-6-azaspiro[3.4]octan-6-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(8-hydroxy-7-oxo-6-azaspiro[3.4]octan-6-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(7-hydroxy-6-oxo-5-azaspiro[2.4]heptan-5-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(6-methyl-2-oxo-1,3-oxazinan-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(4-methyl-2-oxo-1,3-oxazinan-3-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(3S,4R)-3,4-dihydroxy-2-oxo-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(3S,4R)-3-hydroxy-2-oxo-4-pyrimidin-2-yloxy-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-[5-methyl-5-(morpholine-4-carbonyl)-2-oxo-1,3-oxazinan-3-yl]-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-[(2R,3R,4S)-4-hydroxy-2-methyl-5-oxo-3-pyrimidin-2-yloxy-pyrrolidin-1-yl]-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-6-methyl-3-(2-oxo-4-pyrimidin-2-yl-pyrrolidin-1-yl)-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

(6S)-3-(3-hydroxy-2-oxo-4-phenyl-pyrrolidin-1-yl)-6-methyl-N-(3,4,5-trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

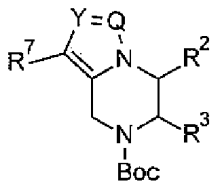
(6S)-3-[(5S)-5-methoxy-2-oxo-1,3-oxazinan-3-yl]-6-methyl-N-(3,4,5trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide; and

(6S)-3-[(5R)-5-methoxy-2-oxo-1,3-oxazinan-3-yl]-6-methyl-N-(3,4,5trifluorophenyl)-6,7-dihydro-4H-pyrazolo[1,5-a]pyrazine-5-carboxamide;

or pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

35. A process for the preparation of a compound according to any one of claims 1 to 34 comprising any of the following steps:

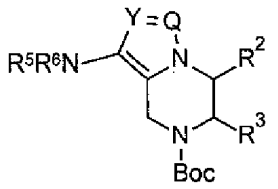
(a) a reaction of a compound of formula (V),



(V),

with an acid followed by urea formation with amine R^4NH_2 in the presence of a phosgene equivalent;

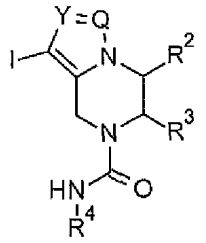
(b) a reaction of a compound of formula (VII),



(VII),

with an acid followed by urea formation with amine R^4NH_2 in the presence of a phosgene equivalent;

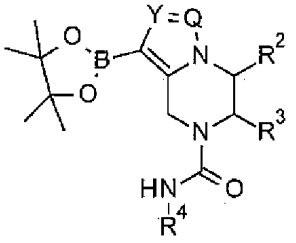
(c) a reaction of a compound of formula (IX),



(IX),

with R^7-$B(OH)_2$; or

(d) a reaction of a compound of formula (X),



(X),

with halide via Suzuki-Miyaura reaction;

wherein R^2, R^3, R^4 are defined as in any one of claims 1 to 34;

R^5 and R^6 together with the nitrogen atom they are attached to form a 3-7 membered heterocyclyl; and

R^7 is aryl or heteroaryl.

36. A compound or pharmaceutically acceptable salts, enantiomers or diastereomers according to any one of claims 1 to 34 for use as therapeutically active substance.

37. A pharmaceutical composition comprising a compound in accordance with any one of claims 1 to 34 and a therapeutically inert carrier.

38. The use of a compound according to any one of claims 1 to 34 for the preparation of a medicament for the treatment or prophylaxis of hepatitis B virus infection.

39. A compound or pharmaceutically acceptable salt, enantiomer or diastereomer according to any one of claims 1 to 34 for use in the treatment or prophylaxis of hepatitis B virus infection.

40. A compound or pharmaceutically acceptable salt, enantiomer or diastereomer according to any one of claims 1 to 34, when manufactured according to a process of claim 35.